VOLUME 43 NUMBER 3

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EFFECTS OF TILTED LENSES

An interesting case has been brought to our attention, the solution of which was a matter of matching the tilt of the spectacles to the tilt of the trial lenses.

The case was one of monocular aphakia and required a + 10.00 + 2.50 cx 180. This correction in the trial frame gave 20/20 vision but in the spectacle frame produced only 20/50 vision.

Lenses were ground that compensated for a vertex distance change but the improvement in acuity was slight.

The solution was simple when it was found that due to facial structure, the trial frame tilted about 15 degrees in respect to the vertical plane. When spectacles were tilted the same amount, the acuity was the same as with the trial lenses.

If it were not practical to tilt the spectacle lenses to the desired angle, the resultant lens power could have been easily calculated. In most cases such a procedure is much more desirable than tilting the lenses.

A workable rule of thumb to determine the effects of tilting a sphere is as follows: A 4.00 D lens tilted 20 degrees produces a .50 cylinder whose axis is toward the tilt. There is, of course, a slight sphere change but of neglible amount.

When determining the effects of tilting a cylinder lens, the axis of the cylinder is a factor, because, for example, a + 4.00 cylinder axis 180 with the top tilted forward 20 degrees, has the power of a + 4.75 cylinder (approximately), while a + 4.00 cylinder axis 90 is not affected by a forward tilt.

The table below shows the effects of tilting both a one diopter sphere and a one diopter cylinder.

Spherical Lens			Cylindrical Lens	
Degrees Tilt	Power Sphere	Induced Cylinder	Degrees Tilt	Power Cylinder
0	1.00	0.00	0	1.00
5	1.00	0.01	5	1.01
10	1.01	0.03	10	1.04
15	1.02	0.07	15	1.10
20	1.04	0.14	20	1.18
25	1.06	0.23	25	1.29

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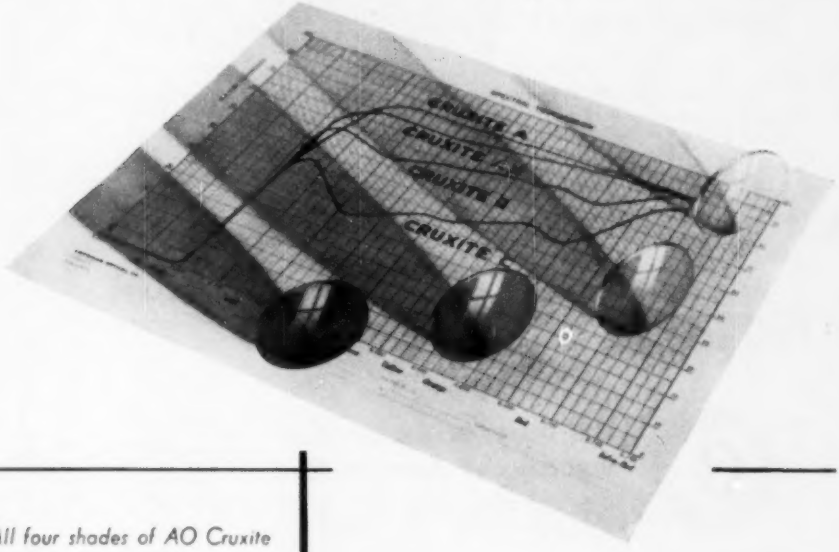

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FOREWORD

This year the Guild of Prescription Opticians of America observes its twenty-fifth anniversary as a national organization.

Starting a quarter century ago with only 17 members along the eastern seaboard in and near Philadelphia where the Guild idea had its inception, today there are 325 members in 34 states from New England to Florida, from the east coast to the west coast, and in Canada.

The Guild started because there was a need for it; common problems and common interests among ethical dispensers who had cast their lot with Medical Eye Care.

The Guild has grown because other ethical dispensers have realized that their own interests and needs were allied with Guild standards and practices.

There is much in the Guild's history that is interesting. And on this page for the balance of our Silver Anniversary year we shall be sharing the Guild's story with you.

It will be briefly written, touching only the high spots. But at the end of this series we believe you will better understand the Guild, its purposes and attainments, and the substantial part it has taken in serving and supporting Medical Eye Care.

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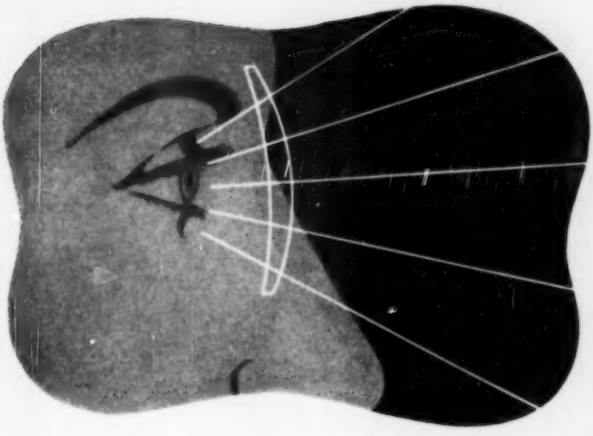

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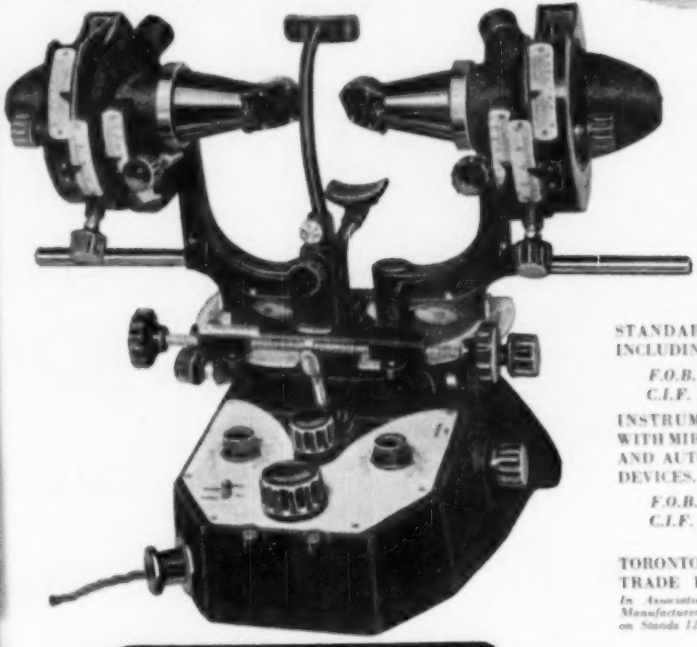

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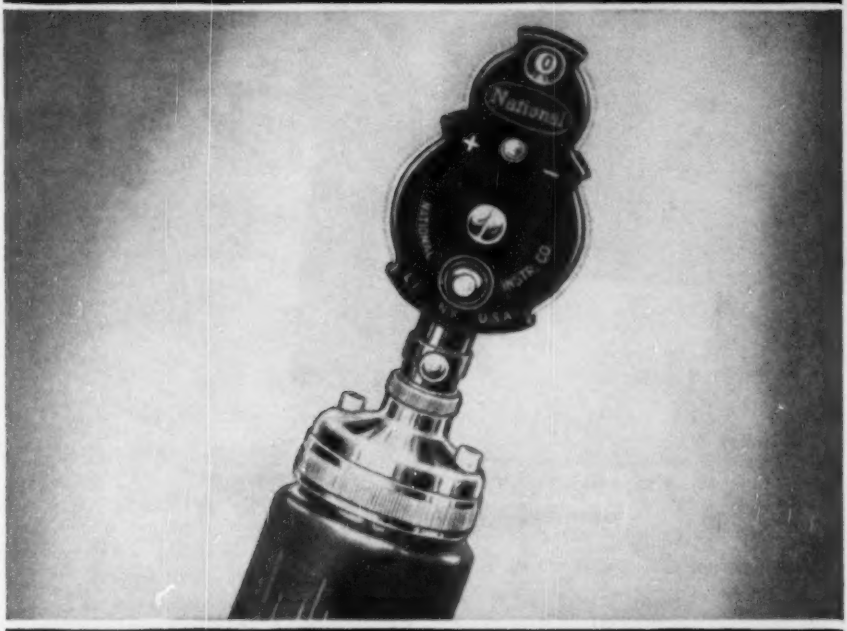

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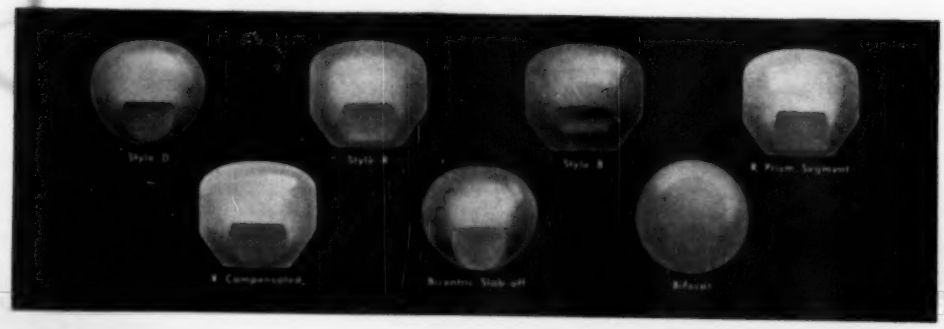

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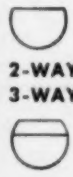

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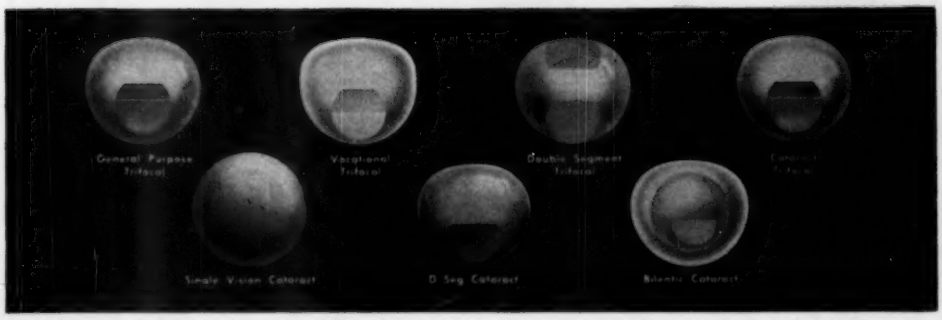

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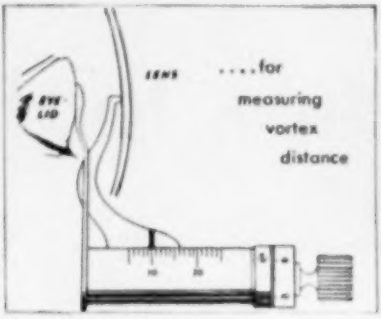

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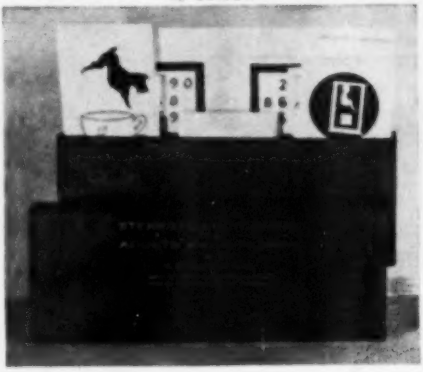

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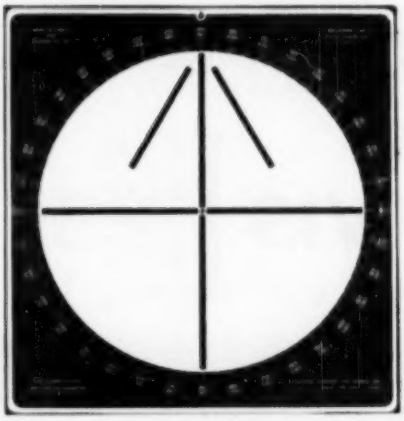

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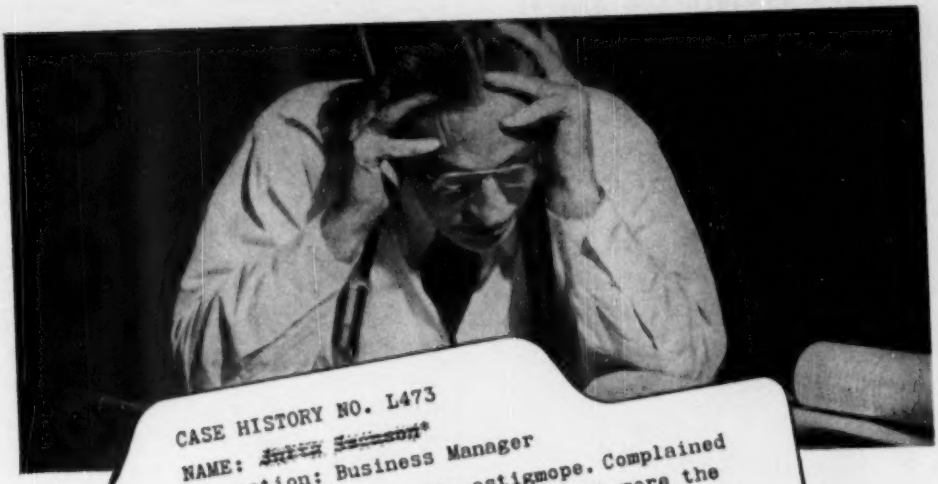

CASE HISTORY NO. L473

NAME: ~~Julia Salmon~~*

Occupation: Business Manager

March 15 -- Hyperopic astigmope. Complained of continuous headaches. Patient wore the following Rx:

+25 Cyl x 180
+50 Cyl x 180 in tint
(TINTED LENSES WORE; DID NOT GIVE NEUTRAL ABSORPTION)

Examination revealed physical correction accuracy.

First Rx

Issued same Rx in white crown.

April 12 -- Patient returned to report headache condition unrelieved. Discussion revealed no extraordinary illumination background. Absorption check test with Soft-Lite Trial Case Accessory indicated need for Soft-Lite #1. Issued the following Rx:

+25 Cyl x 180
+50 Cyl x 180 Soft-Lite #1

Second Rx

April 24 -- Patient returned for re-check. Reported that headaches were completely banished.

*NAME ON FILE WITH SOFT-LITE LENS CO., INC.

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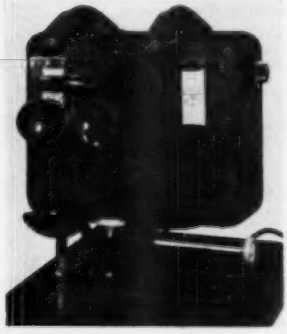

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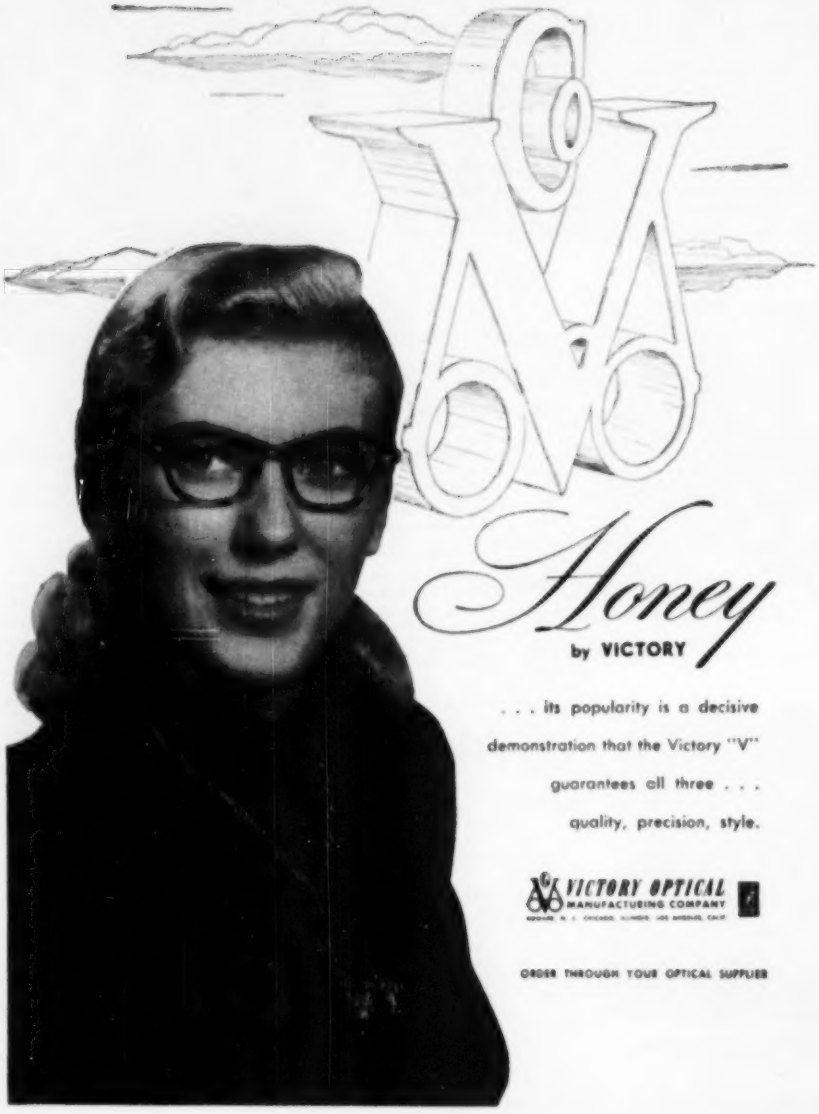

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VOLUME 43 MARCH 1950 NUMBER 3

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LATE FISTULIZATION OF OPERATIVE WOUNDS

Diagnosis and Treatment

JOHN H. DUNNINGTON, M.D.
NEW YORK
AND
ELLEN F. REGAN, M.D.
FRAMINGHAM, MASS.

AMONG the postoperative complications of intraocular surgery, those of late fistula formation and hypotony have received relatively little attention. We desire to emphasize a type of slowly leaking cicatrix, to describe the associated symptom complex and to present a method of therapy which we have found successful.

Owing to imperfect closure, any penetrating wound of an eyeball, either traumatic or surgical, may be followed by a cystoid scar. The creation of such a cicatrix is in some instances the aim of the surgeon, while in others the condition occurs when least desired. If such a cicatrix opens to the surface, a fistula is produced. This fistulous tract may be large or small. It may be constantly open, or it may be closed at times and open at others. The clinical appearance of the usual form, in which the fistula is large and open at all times, is well known. The eye is congested and soft. The cornea is often hazy, with stromal striae and the folds in the posterior elastic lamina (Descemet's membrane). The anterior chamber is absent, and the iris is in contact with the posterior surface of the cornea. Either the anterior surface of the lens or that of the vitreous is often in apposition with the endothelial surface of the cornea. A choroidal detachment is usually present. This condition is most commonly seen soon after operation, but occasionally it occurs later in the postoperative course. Its diagnosis, treatment and consequences are well recognized and will not be discussed further at this time. In those cases in which there is slow or intermittent leakage of the aqueous the signs and symptoms, while less obvious than those just described, are none the less characteristic. A survey of the literature shows that but little attention has been directed toward the diagno-

Read at the Eighty-Fifth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 2, 1949.

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology of the Presbyterian Hospital in the City of New York.

sis and treatment in this group. Kirby [1] described the symptoms along with those associated with delayed wound healing after cataract extraction. Barkan [2] described similar findings in connection with late hypotony after trephining, but he did not attribute them to the presence of a leaking cicatrix. O'Brien [3] referred to the minuteness of the opening in the wound in some cases of choroidal detachment. A brief report on this symptom complex was made by one of us (J.H.D.) [4] as part of a discussion on hypotony at the annual meeting of the American Academy of Ophthalmology and Otolaryngology in 1947.

SIGNS AND SYMPTOMS

The usual history in cases of this condition is that of an uneventful intraocular operation and a quiet postoperative course. Often a slightly irregular pupil or an incarcerated iris pillar and a small cystoid scar are present, but the visual acuity after operation is good and the general appearance of the eye is satisfactory. Such a state may continue for weeks, or even months. Then the patient returns complaining of tearing, intermittent blurring of vision and a dull ache about the eye. The symptoms are often transient, and occasionally, as noted in 1 of the cases, they are worse on awakening in the morning. In the beginning the outstanding complaint is a watery eye, while later blurring of vision and actual discomfort are frequently noted.

In the early stages the findings are as follows: There is profuse lacrimation in an eye that to casual inspection appears normal. The globe is not injected; the cornea is clear, and the anterior chamber is normal in depth and free from cellular deposits. On digital palpation, however, the ocular tension is found to be reduced and slight ciliary tenderness is elicited. In some instances the hypotony is so profound that the tonometer does not register the pressure. Examination of the wound frequently reveals a cystoid area of the conjunctiva that is soft and pits on pressure, while in some cases the wound appears flat and the tiny opening escapes detection. If one places a drop of fluo-

1. Kirby, D. B.: Prevention and Handling of Complications Arising During and After Cataract Extraction: Some Practical Points, Arch. Ophth. **25**:866-901 (May) 1941.

2. Barkan, H.: Use of the Shahan Thermophore in Hypotony of the Eyeball as a Result of the Elliot Trephining Operation, Am. J. Ophth. **23**:692-693 (June) 1940.

3. O'Brien, C. S.: Detachment of the Choroid After Cataract Extraction: Clinical and Experimental Studies, with a Report of Seventy-Five Cases, Arch. Ophth. **14**:527-540 (Oct.) 1935.

4. Dunnington, J. H., in discussion on Heath, P.: Ocular Hypotony, Tr. Am. Acad. Ophth. **52**:613-621 (July-Aug.) 1948.

rescein on the suspected area and then applies gentle but firm pressure to the globe, a leakage of aqueous is usually demonstrable. Since these fistulous cicatrices are at times covered by a thin layer of conjunctival epithelium, this test does not invariably give a positive result. Repeated examinations are occasionally required to establish the intermittent nature of the leakage of aqueous. In a few instances it is even necessary to dissect up the conjunctiva to be certain of the exact site of drainage. If the anterior chamber becomes shallow with the application of pressure to the globe, it is corroborative evidence of slow fistulization.

Should such a situation be permitted to continue, the visual acuity will decrease and the patient's symptoms will become severe, resembling in every detail those found in low grade iridocyclitis. At this stage, examination with the corneal microscope will reveal a slight flare and a few cells in the anterior chamber. There may be an increase in the number of opacities in the anterior vitreous. These findings have led many to diagnose the condition as iridocyclitis and to persist in the treatment of the secondary uveal inflammation without taking into account the primary cause of this continued irritation. If the hypotony persists, edema of the optic nerve may ensue, or, as in 1 of our cases, there may be sufficient edema of the retina in the macular region to simulate a flat detachment of the retina. It is interesting to note that in none of the 15 cases here reported was a detachment of the choroid present.

A late complication of more serious import is epithelization of the anterior chamber. This was seen in 1 of the cases reported here. Both Vail [5] and Theobald and Haas [6] emphasized the importance of delayed wound healing in the production of epithelization of the anterior chamber, and Calhoun [7] reported that in 10 of the 19 cases of epithelization which he observed leakage of aqueous was demonstrable with the fluorescein test at some time. Late infection is always a danger in the presence of a fistula. In 2 cases in our series early endophthalmitis was observed, and in a third case, not included because no treatment was given, the eye was lost because of panophthalmitis.

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5. Vail, D.: Epithelial Downgrowth into the Anterior Chamber Following Cataract Extraction Arrested by Radium Treatment, Tr. Am. Ophth. Soc. **33**:306-325, 1935.

6. Theobald, G. D., and Haas, J. S.: Epithelial Invasion of the Anterior Chamber Following Cataract Extraction, Tr. Am. Acad. Ophth. **52**:470-485 (May-June) 1948.

7. Calhoun, F. P., Jr.: Personal communication to the authors on the clinical recognition and treatment of epithelization of the anterior chamber following cataract extraction.

TREATMENT

Discussions of the treatment of fistulizing wounds, especially the late treatment, have appeared sporadically in the literature for many years. Earlier writers spoke of filtering cicatrices after cataract operation as "safety valves" for the prevention of glaucoma (Ayers[8]). Both Spaeth[9] and Kirby[10] pointed out the danger of glaucoma resulting from closure of a slowly leaking fistula. Furthermore, Kirby[10] stated that if a fistula is present and the ocular tension normal, glaucoma will occur if the opening is obliterated. In our experience, postoperative glaucoma has not been an important factor, and the sequelae of an untreated filtering cicatrix are such that closure should be considered carefully in all cases.

The following methods of treatment of fistulizing wounds with hypotony have been proposed:

Medical or Expectant Treatment.—This has been suggested by Gradle,[11] Spaeth[12] and Wright[13] in the form of local applications of ethylmorphine hydrochloride ("dionin"), atropine sulfate, hot compresses and pressure dressings. However, since such medication does not help the primary difficulty, namely, imperfect closure of the wound, it is unlikely that it will be efficacious, and watchful waiting is too dangerous a policy to follow.

Cautery.—The application of some form of cautery to flatten the cystoid area has been advised for many years. Meller[14] recommended the use of a hot probe in cases of delayed reformation of the anterior chamber and leakage of aqueous, as demonstrated with the fluorescein test, after cataract extraction. The electric cautery for prolapse of

8. Ayers, S. C.: Glaucoma After Cataract Operations, Arch. Ophth. **26**:208-213, 1897.

9. Spaeth, E. B.: The Management of Some Complications Which Follow Cataract Extraction, Am. J. Ophth. **23**:1019-1028 (Sept.) 1940.

10. Kirby, D. B.: Fistulizing Cicatrices and Prolapse of the Iris Following Imperfect Healing of the Incision for Extraction of Cataract, Virginia M. Monthly **66**:711-716 (Dec.) 1939.

11. Gradle, H. S.: The Closure of Traumatic Subconjunctival Corneoscleral Fistula, Arch. Ophth. **50**:154-157 (March) 1921.

12. Spaeth, E. B.: The Principles and Practice of Ophthalmic Surgery, ed. 3, Philadelphia, Lea & Febiger, 1944, pp. 673-677.

13. Wright, R. E.: Lectures on Cataract: III. Anterior-Segment and Other Complications in the Post-Operative Period, Am. J. Ophth. **20**:240-253 (March) 1937.

14. Meller, J.: Augenärztliche Eingriffe; eine kurzegefasste Operationslehre, ed. 4, Vienna, Julius Springer, 1938, pp. 227-228.

the iris was advocated by Gala [15] and many others. Bulson,[16] Magitot and Dubois-Poulsen,[17] Bothman [18] and others stated that they prefer to cauterize with trichloroacetic acid. Gifford [19] and Gradle [11] both warned that with the use of this acid sympathetic ophthalmia may occur and suggested that it never be employed in the treatment of prolapse of the iris unless the treated area is covered with a conjunctival flap. Wiener and Alvis [20] favored repeated applications of 10 per cent silver nitrate to cystoid scars producing hypotony. Albrich [21] reported successful results following applications of diathermy to the area of filtration when vitreous is beneath the conjunctiva. Barkan [7] found treatment of the cystoid cicatrix with Shahan's thermophore helpful in cases of late hypotony after trephining. There is no doubt that cauterization of the wound will in certain instances produce a firm cicatrix, but it is not an exact method.

The Free Graft.—The difficulty in securing permanent closure of these fistulous tracts has caused some surgeon to advocate suturing a free graft of tissue subconjunctivally over the area of drainage. Such treatment has been used chiefly to correct hypotony after trephination. For this purpose, Bothman [18] used a graft excised from the superior rectus muscle near its insertion, while Wilmer [22] and Magitot and Dubois-Poulsen [17] grafted a piece of Tenon's capsule over the trephine opening. We have had no experience with this form of therapy.

Conjunctival Flap.—Probably the most widely accepted method of treating a filtering cicatrix is the use of a Kuhnt or Van Lint type of conjunctival flap. Many writers, including Herbert,[23] have advocated the use of such a flap in the repair of a cystoid cicatrix. The method

15. Gala, A.: Treatment of Postoperative Complications After Extraction of Cataract. Bratisl. lekár. listy **11**:513-516 (Nov.) 1931.

16. Bulson, A. E., Jr., cited by Gifford, H.: The Danger of Sympathetic Ophthalmia from the Use of Cautery on Treating Iris Prolapse: Other Methods of Treatment, J. A. M. A. **55**:386-388 (July 30) 1910.

17. Magitot, A., and Dubois-Poulsen, A.: Traitement des prolapsus iriens par l'acide trichloeroacétique (technique de Bettman et Barkan), Ann. d'ocul. **175**:449-454 (June) 1938.

18. Bothman, L.: Repair of Choroidal Detachment: Report of a Case, Arch. Ophth. **18**:65-67 (July) 1937.

19. Gifford.[16]

20. Wiener, M., and Alvis, B. Y.: Surgery of the Eye, Philadelphia, W. B. Saunders Company, 1939.

21. Albrich, K.: Zur Behandlung des subkonjunktivalen Glaskörpervorfalls, Klin. Monatsbl. f. Augenh. **93**:663-665 (Nov.) 1934.

22. Wilmer, W. H.: Discussion on the Results of Operative Treatment of Glaucoma, Tr. Ophth. Soc. U. Kingdom **47**:230-262, 1927.

23. Herbert, H.: Discussion on Post-Operative Complications of Cataract Extraction, Tr. Ophth. Soc. U. Kingdom **34**:51-55, 1914.

described by Wheeler [24] has been recommended by Goar,[25] Kirby,[19] Cornet,[26] Workman [27] and others. In 1936 Verhoeff [28] wrote of using a large Van Lint flap in 2 cases in which the conjunctival flap he employed for trephining had retracted. This method will doubtless cure many of these cicatrices, but in our hands it has not proved uniformly successful.

Suturing of the Fistula.—It is our belief that a successful closure of a fistula is more certain if, in addition to use of a conjunctival flap for covering the wound, the corneal and scleral lips of the tract are approximated by suturing. This is not a new method of therapy, but it has received relatively little attention. In 1920 Gradle [11] described its use in the late treatment of 2 cases of traumatic fistula. His technic was very similar to the one we suggest. The attention of one of us (J. H. D.) was first called to the value of such suturing in 1929. At that time, some months after an uneventful cataract extraction, there developed a fistulizing cicatrix in which leakage was demonstrable by the fluorescein test. Two attempts were made to close the fistula by the usual conjunctival flap method. Then the late Dr. John M. Wheeler successfully closed the fistula by combining a conjunctival flap with suture of the fistulous opening.

TECHNIC

A conjunctival incision is made immediately surrounding the fistulous opening (figure, *1*). After the area of the fistula is outlined in this manner, a conjunctival flap is dissected up from the limbus. This flap is made large enough to cover the upper corneal limbus for about 2 mm. On the completion of this dissection, a conjunctivoepiscleral suture is placed near the limbus below the limit of the flap and then passed through the corresponding edge of the prepared flap. These sutures are then held taut to be certain that the flap will cover the fistula and the upper corneal margin. The sutures are then released, and the originally outlined fistulous tract with the surrounding conjunctival epithelium is excised. At this point the fistulous opening is inspected; should iris be prolapsed, it is excised. The edges of the opening are then freshened up and usually touched with a hot probe, and a double-armed fine black silk suture is passed through the lips of the fistula (figure,

24. Wheeler, J. M.: The Collected Papers of John Martin Wheeler, M.D., on Ophthalmic Subjects, New York, Columbia University Press, 1939.

25. Goar, E. L.: Management of the Complications of Intraocular Surgery, Am. J. Surg. **42**:62-68 (Oct.) 1938.

26. Cornet, E.: Le recouvrement conjonctival à sutures conjonctivo-épiscléral es et conjonctivo-cornéennes, Ann. d'ocul. **176**:550 (July) 1939.

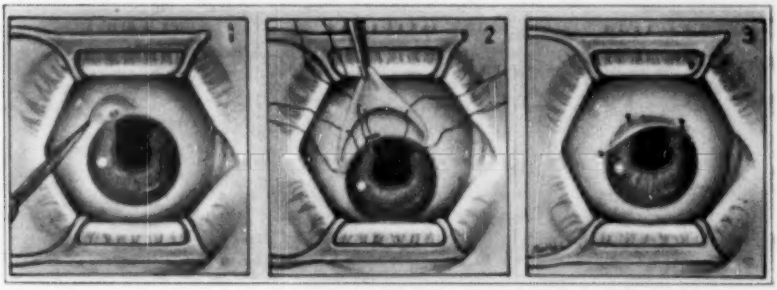
27. Workman, J. B., Jr.: Conjunctival Plastic Operation in Cases of Hypotonia from Filtering Operations or Ocular Fistulae, J. South Carolina M. A. **37**:249-250 (Sept.) 1941.

28. Verhoeff, F. H.: A New Conjunctival Flap for Trephining Operations, Am. J. Ophth. **19**:46 (Jan.) 1936.

2). The conjunctival flap is next drawn down and the traction sutures are tied. The double-armed corneoscleral suture is then passed through the overlying conjunctiva and tied (figure, *3*). A monocular dressing is applied and changed every forty-eight hours. The sutures are removed on the fifth day. The postoperative course has been quiet in all cases.

REPORT OF CASES

CASE 1.—Mr. V. M., aged 56, was first seen in April 1937, complaining of a blurred, sensitive right eye. He gave a history of having had an extracapsular cataract extraction with complete iridectomy in September 1935 and an apparently uneventful recovery until May 1936, when a conjunctival flap was drawn over a fistulous wound. Examination showed that vision was limited to perception of hand movements with accurate light projection; the cornea was clear; the anterior chamber was clear and of normal depth; the secondary membrane was faint; the nasal iris pillar was incarcerated, with an area of subconjunctival infiltration above; tension was too low to be recorded. The next day the cicatrix was excised; the



Stages in closure of operative fistula.

edges of the wound were curetted, and a conjunctival flap was drawn over the area of filtration. The edges of the fistula were not sutured. Tension remained low, and one week later another conjunctivoplasty was performed, with suturing. Tension rose to normal; vision was 20/40, but a cystoid scar remained. The patient returned in November 1938 with the complaint of blurred vision in the right eye for three days. Examination showed edema of the lids, conjunctival injection with a probable abscess under the flap at 12 o'clock, radial white lines in the deeper layers of the cornea and normal tension. Infection subsided quickly under treatment, and vision was 20/40. The flap was very thin; a fistula was present, and another conjunctivoplasty with suturing of the fistula was done on Dec. 14, 1938. Six days later there was a rise in tension, which was controlled by installation of 2 per cent pilocarpine hydrochloride four times a day. Two weeks later, vision was 20/40, and tension was normal without miotics. The findings were unchanged until the patient's death, in 1945.

Comment.—This case presents several interesting features: (1) Two conjunctival flaps failed to close the fistula; (2) the first suturing partially closed the fistula for two years; (3) resuturing obliterated

the fistula, and the eye retained normal ocular tension and vision of 20/40+ until the patient's death.

CASE 2.—Mr. A. E. P., aged 74, had an intracapsular cataract extraction performed on his right eye on May 26, 1943 (preliminary iridectomy elsewhere), convalescence was uneventful, and postoperative vision was 20/20. On Nov. 23, 1943 he complained of intermittent blurring of vision and watering of this eye on awakening. Examination revealed a filtering cicatrix around the temporal pillar of the iris. On December 1, he complained that the eye was painful. The bleb had ruptured. Signs of early endophthalmitis subsided after antibiotic therapy, and 20/30 vision was obtained. The cystoid cicatrix remained, and the eye continued to water. He refused to have an operation until Sept. 10, 1945, when a conjunctivoplasty with suturing of the fistula was done. The patient has been asymptomatic, tension normal and vision 20/30 since closure of the fistula.

Comment.—This case illustrates the rapidity with which exogenous infection can occur on rupture of the bleb. Furthermore, it is interesting to note that with the subsidence of the infection there was a prompt return of the annoying symptoms, the slow leakage of aqueous, and that these, in turn, promptly disappeared with closure of the fistula.

CASE 3.—Mr. H. H., aged 64, was first seen Sept. 17, 1946, complaining of tearing and loss of vision and the visual field in the left eye. He gave a history of extracapsular cataract extraction with complete iridectomy on April 25, 1946, with corrected postoperative vision of 20/50. On examination he was found to have corrected vision of 10/200, tension of 5 mm. of mercury (Schiøtz), a white eye, a few fine deposits on the posterior surface of the cornea, a few floaters in the anterior chamber, a secondary membrane with good central opening, many moderate-sized opacities in the vitreous, some old chorioretinitis nasal to the disk, retinal edema and elevation below and temporal to the disk and constriction of the field, pronounced above. In the center of the wound, at 12 o'clock was a filtering cicatrix (fluorescein test). Conjunctivoplasty with suturing of the fistula, on September 20, resulted in tension of 22 mm. of mercury (Schiøtz) and vision of 20/50. At the time of writing, vision was 20/40, tension was still normal and the defect in visual acuity was due largely to old chorioretinitis.

Comment.—This instructive case illustrates the changes that may occur in an eye with prolonged hypotony. Correction of this condition brought about prompt restoration of function.

CASE 4.—Mr. S. N., aged 68, had an intracapsular cataract extraction with peripheral iridectomy performed on his left eye on Dec. 19, 1945. The postoperative course was uneventful, and corrected vision was 20/25+. One year later he complained of blurred vision, but the eye appeared normal and vision was still 20/25. On Nov. 7, 1947 he returned because of tearing and difficulty in reading. Corrected vision was 20/50; tension was low; the lips of the incision were not in good apposition at 11 o'clock; the nasal pillar of the iris was adherent to the cornea there, and a fine, thin membrane was seen on the posterior surface of the cornea at 11 to 12 o'clock. One month later the tension was still low, and on pressure aqueous was seen to escape from the wound at 11 o'clock. Conjunctivoplasty, suturing of the fistula and iridectomy were done. Examination of the excised iris tissue showed epithelization of the anterior chamber. Tension remained about 12 mm. of mercury

(Schiøtz); there was no evidence of filtration, and in July 1948 a series of roentgen treatments were given because of increased epithelization. Bullous keratitis developed, and vision is now 3/200.

Comment.—This case is presented to show the necessity of early diagnosis and prompt treatment. Failure to recognize the initial symptoms led to this unsatisfactory result.

CASE 5.—Mr. E. O., aged 55, had a preliminary iridectomy performed on his right eye in December 1928 and an extracapsular cataract extraction in February 1929. A large postoperative hyphemia gradually absorbed, and vision of 20/20— was obtained. In April 1929 the patient complained of tearing and failing vision. Tension was too low to register; there was slight pitting edema at the limbus superiorly, and leakage of aqueous occurred through this fistulous tract. Two attempts to cover the fistula with a conjunctival flap were unsuccessful, and on May 16, 1929 Dr. John M. Wheeler performed a conjunctivoplasty combined with suturing of the fistula. The tension rose to 17 mm. of mercury (Schiøtz); vision improved to 20/15—2, and the eye has remained in this condition.

CASE 6.—Mr. C. L., aged 68, had an iridencleisis performed on his right eye for chronic wide angle glaucoma on September 1943. A shallow anterior chamber and choroidal detachment persisted for six weeks. Then the eye became quiet, tension was normal and the preoperative vision of 15/200 was unchanged. Six months later vision became more blurred. Examination showed a large thin cystoid cicatrix above the scar, tension of 12 mm. of mercury (Schiøtz) and no demonstrable leakage of aqueous. Conjunctivoplasty with suturing of the fistula found at the time of operation was done. Tension rose to 34 mm. of mercury (Schiøtz) but was easily controlled by installation of 2 per cent pilocarpine hydrochloride three times a day. Since May 1944 tension has remained normal, but visual acuity has decreased to 3/200.

CASE 7.—Mrs. D. D., aged 66, had a trephination with peripheral iridectomy performed on her left eye for chronic wide angle glaucoma in May 1942. Ten months later she complained of tearing, but examination showed a quiet eye with tension of 19 mm. of mercury (Schiøtz). In April 1945 she again complained of tearing and of blurred vision. Examination revealed no change in visual acuity; ocular tension was 10 mm. of mercury (Schiøtz); there was mild circumcorneal injection; the anterior chamber was shallow, and leakage of aqueous from the filtering cicatrix could be demonstrated with fluorescein. Conjunctivoplasty with suturing of the wound was done. Tension rose to 53 mm. of mercury (Schiøtz) but was controlled with 2 per cent pilocarpine hydrochloride, instilled three times a day. The patient was not seen again until November 1948 (in the interim she had had an iris inclusion operation, a cataract extraction and cyclodialysis elsewhere on the left eye), at which time she was using furfuryl trimethylammonium iodide (furmethide®) four times a day and physostigmine ointment each night. Tension was 20 mm. of mercury (Schiøtz); corrected vision was 20/40; the anterior chamber contained vitreous; the iris pillars were incarcerated, and the optic disk and visual fields were unchanged.

CASE 8.—Mr. G. W., aged 50, had a trephination with peripheral iridectomy performed on each eye for chronic wide angle glaucoma in November 1939. The anterior chamber of the left eye did not reform for fourteen days. In April 1945 the patient complained of pain in the left eye. Examination showed mild conjunctival injection; vision was 20/15—; tension was 6 mm. of mercury (Schiøtz), and there was a filtering cicatrix with a very thin covering of conjunctiva. Silver

nitrate, 1 per cent, was applied to the cicatrix. The eye became white; there was no evidence of leakage of aqueous, but the tension was too low to register on the tonometer. On May 9, 1945, a conjunctivoplasty with suturing of the fistula disclosed at operation was performed, and the tension became 15 mm. of mercury (Schiøtz). Vision and tension have remained normal, and there has been no change of field since operation.

Case 9.—Mr. C. D., aged 52, had an intracapsular cataract extraction with two peripheral iridectomies performed on his left eye on June 23, 1943. The anterior chamber did not reform until the seventh postoperative day; and an anterior synechia, extending from 12 to 1:30 o'clock and involving the full radius of the iris, developed. Tension was normal and vision was 20/15. In December 1943 the patient complained of tenderness and blurring of vision of the left eye. The eye appeared quiet, vision was 20/15 and tension was normal. In May 1944 tension was very low but other findings were unchanged. The symptoms persisted, but the tension and appearance of the eye remained normal until October 31, when the patient complained of pain, photophobia and blurred vision. Examination revealed a cystoid cicatrix extending from 2 to 3 o'clock at the limbus, a normal interior of the eye and very low tension, but no definite leakage of aqueous. Six weeks later the tension was still low, vision was 20/70—, the anterior chamber was shallow and leakage of aqueous from the filtering cicatrix was demonstrable with fluorescein. On Dec. 7, 1945 a conjunctivoplasty with suturing of the fistula was done. One month later tension was 41 mm. of mercury (Schiøtz). Miotics have been used successfully, with only occasional rises in pressure. Vision is 20/20—; there is cupping of the disk, and a nasal step is present in the field.

Case 10.—Mrs. A. M., aged 62, had an attempted intracapsular cataract extraction with complete iridectomy on her right eye in July 1944. There was difficulty in inserting a postplaced corneoscleral suture at 11 o'clock. In November 1944 the patient complained of intermittent pain and tearing. Examination revealed a very small, thin filtering cicatrix at the limbus at 11 o'clock with the temporal pillar of the iris incarcerated there. The symptoms persisted, but tension remained normal and leakage of aqueous could not be demonstrated with fluorescein. In December 1945, tension was low, vision was 20/20—2 and there was a fistula in the area of the cicatrix, through which leakage of aqueous was shown with fluorescein. A conjunctivoplasty with suturing of the fistula was performed. Tension rose to 35 mm. of mercury (Schiøtz) but returned to normal without the use of miotics. The patient is now comfortable; tension is normal; vision is 20/20—2, and there has been no recurrence of the filtering cicatrix.

Case 11.—Mrs. A. H., aged 65, had an intracapsular cataract extraction with peripheral iridectomy performed on her left eye in January 1946. A small anterior peripheral synechia developed at 1:30 o'clock. In September 1946 the patient complained of pain, irritation and black spots. Vision was 20/25+; tension was 13 mm. of mercury (Schiøtz); there were fine opacities in the vitreous, and a filtering cicatrix was present at 11 o'clock. Results of examination were unchanged, but the patient complained of blurred vision and tearing until July 2, 1947, when a conjunctivoplasty was performed. After the cicatrix was excised, a fistula seen at the limbus was sutured. The cicatrix has not recurred; the patient is comfortable; tension is normal, and vision is 20/15.

Case 12.—Mrs. J. S., aged 47, was first seen in November 1947, complaining of failing vision, discomfort and tearing. Two years previously she had had an extracapsular cataract extraction with complete iridectomy elsewhere. Examination showed vision of 20/40+ and tension of 5 mm. of mercury (Schiøtz). Both iris

pillars were incarcerated in the cataract section; there was a large filtering cicatrix with a thin conjunctival covering above the superior limbus, but no leakage of aqueous was demonstrable. Conjunctivoplasty was performed on Dec. 10, 1947. A fistula found beneath the conjunctiva in the area of the old cataract section was sutured. Tension rose to normal; vision is now 20/25, and there has been no recurrence of the cicatrix.

Case 13.—Mrs. J. N., aged 62, had an intracapsular cataract extraction with peripheral iridectomy performed on her left eye in May 1947. The pupil was updrawn at the first dressing, and a small subconjunctival prolapse of the iris was present in the wound at 1 o'clock on the eighth day. A cystoid cicatrix developed in the area of the prolapsed iris; vision was 20/40, and the patient could read the smallest print. In February 1948 she returned, complaining of tearing and difficulty in reading. Vision was 20/70, and she read Jaeger type 9 with difficulty. Tension was low; the anterior chamber and fundus were normal. In the area of the cystoid scar at 12 o'clock a leaking fistula was demonstrated with fluorescein. Conjunctivoplasty with suturing of the fistula and complete iridectomy of the prolapsed iris were done. Tension is normal; vision is 20/40, and there has been no recurrence of the cystoid cicatrix.

Case 14.—Mrs. N. T., aged 72, was first seen in December 1948, complaining of tearing and aching of the left eye. She gave a history of intracapsular cataract extraction with complete iridectomy on May 1948. Examination showed corrected vision of 20/20, tension of 10 mm. of mercury (Schiøtz), a deep anterior chamber and incarceration of the temporal pillar of the iris in the wound. A cystoid cicatrix, 5 by 3 mm., was present between 11 and 12 o'clock at the limbus, and through this an opening in the wound could be seen. Genioscopy showed that the synechias were present only at the edges of the pillar and the iris stump. Conjunctivoplasty with suturing was done on Dec. 15, 1948. When last seen, two months after operation, the patient was comfortable; vision was 20/20; tension was 15 mm. of mercury (Schiøtz), and the conjunctiva at the upper limbus was flat and the wound firmly closed.

Case 15.—Mrs. C. W., aged 64, was first seen in January 1949, with the complaint of tearing, blurred vision and some intermittent photophobia. She gave a history of intracapsular cataract extraction with complete iridectomy on the left eye, in May 1948. Examination showed vision of 20/25—, low tension, and incarceration of the iris pillars. A large filtering cicatrix extended from 12 to 2 o'clock, where the edges of the cataract section were in poor apposition and were lined with iris tissue. Vitreous filled most of the anterior chamber but was not in contact with the cornea. Leakage of aqueous was demonstrated with fluorescein, after which the vitreous was seen in apposition with the posterior surface of the cornea. Conjunctivoplasty with suturing of the fistula was done. The patient is now comfortable; tension and vision are normal, and there has been no recurrence of the filtering cicatrix.

RESULTS

The surgical procedure described has been used in 15 cases. In 1 of them the original operation was an iridencleisis; in 2, a trephining, and in 12, a cataract extraction. Analysis of the results obtained shows that in 13 cases the fistula was closed and useful vision restored. In 1 instance a cystoid scar persisted and eighteen months later fistulization recurred. A second conjunctivoplasty with suturing resulted in firm closure, with obliteration of the filtering cicatrix. In 2 other

cases satisfactory closure of the fistula was affected but the vision gradually failed. In 1 of them coexisting epithelization of the anterior chamber was responsible for the visual loss, while in the other case, one of advanced glaucoma, vision continued to deteriorate in spite of restoration of normal ocular tension. In 5 instances the operation was followed by glaucoma. In 2 of these 5 cases the rise in ocular tension was evidently transitory, because after use of miotics for a few days the ocular tension became normal and has remained so without medication. In 2 other cases the ocular tension has been controlled by the continued use of moitics, while in 1 case it has been normalized by a second operation for glaucoma (the original procedure was a trephining) performed elsewhere two years after the closure of the fistula.

SUMMARY

The signs and symptoms of slow or intermittent leakage of aqueous are characteristic. Lacrimation, blurred vision and hypotony, all of which may be intermittent, are most suggestive of fistulization, even though the anterior chamber is normal in depth. Since the fluorescein test does not always demonstrate leakage of aqueous, repeated examinations may be necessary to establish the diagnosis. Prompt treatment affects a cure. In our hands, the method of choice has been a combination of cauterizing the opening, suturing its edges and covering it with a conjunctival flap.

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TREATMENT OF RETINITIS PIGMENTOSA WITH COD LIVER OIL INJECTIONS AND PLACENTAL IMPLANTATION

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NEW YORK

THE UNSATISFACTORY status of the current treatment of retinitis pigmentosa is too well known to need emphasis; hence any treatment reliably reported to be effective is worthy of investigation. It is the purpose of the present study to evaluate the treatment with cod liver oil and placental implantations which was reported by Filatov and his co-workers [1] to be highly successful. A brief survey of the literature follows. For a more complete history, the reader is referred to the valuable papers of Gordon.[2]

The theory that the disease is dependent on choroidal sclerosis and attenuation of the retinal arteries has led to various attempts at vasodilation. Duke-Elder [3] summarized the host of experiments in this direction by stating that, "while their practice frequently leads to some transient improvement, doubtless owing to the increased circulation and

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This investigation was made with the assistance of a grant from the Committee on Therapeutic Research, Council on Pharmacy and Chemistry, of the American Medical Association. The American-Soviet Medical Society and several private contributors supplied additional funds.

1. (*a*) Filatov, V. P.: Tissue Therapy in Ophthalmology, Am. Rev. Soviet Med. **2**:53, 1944; (*b*) Retinitis Pigmentosa, ibid. **3**:395, 1946; (*c*) Implantation of Preserved Placenta in Retinitis Pigmentosa, ibid. **3**:397, 1946. (*d*) Filatov, V. P., and Verbitska, V. A.: Treatment of Retinitis Pigmentosa with Intramuscular Injections, ibid. **3**:388, 1946; (*e*) Implantation of Preserved Liver in Retinitis Pigmentosa, ibid. **3**:398, 1946.

2. Gordon, D. M.: (*a*) Treatment of Retinitis Pigmentosa with Special Reference to the Filatov Method, Am. J. Ophth. **30**:565, 1947; (*b*) Experimental Treatment of Retinitis Pigmentosa, Tr. Am. Acad. Ophth. **52**:191, 1948.

3. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1947, vol. 3, p. 2781.

metabolic activity excited in the eye, the ultimate results have been disappointing." Biró,[4] using amyl nitrite, noted improvement in 5 of 13 cases. When amyl nitrite was used in conjunction with liver extract, improvement resulted in 2 of 5 cases. He stated the belief that here, as with other cases in which ovarian and testicular extract was used, dominant-inherited retinitis pigmentosa was milder and more easily influenced than the recessive type. Brown,[5] using retrobulbar injections of atropine to secure increased circulation to the choriocapillaris, noted improvement in 2 of 6 cases. He injected 1 cc. of a 1:1,000 dilution of atropine sulfate into the muscle cone twice a week.

The apparent, partial success with transient dilatation by drugs was logically followed by attempts at permanent dilatation of the retinal and choroidal vessels by section of the sympathetic nerve supply. Many papers on this method have appeared in the last twenty years, of which the following authors may be mentioned. Meighan [6] reported only slight improvement after unilateral extirpation of the superior and middle cervical ganglions on one side in a man aged 20. Campbell,[7] after unilateral cervical ganglionectomy on a woman aged 24, found a post-treatment gain in the upper half of the visual fields. MacDonald and McKenzie [8] reported 4 cases. In 1 case the sympathetic trunk was divided below the second thoracic ganglion, while in the other 3 cases the stellate ganglion and the intervening portion of the sympathetic trunk were removed in addition. They noted only slight improvement in 2 of the 4 cases and stated the belief that results were better when the operation was performed earlier. Kerr [9] noted improvement in 3 of 8 cases following removal of both superior cervical ganglions and all of their branches. In the 3 cases with improvement vision was only moderately impaired prior to operation, while in the 4 cases without improvement the disease was in an advanced stage. Kerr concluded that superior cervical sympathectomy gives the only chance for improvement in retinitis pigmentosa, provided that the pathologic process has not advanced so far as to reduce vision below one tenth of normal. Also, those cases in

4. Biró, I.: Therapeutic Experiments in Cases of Retinitis Pigmentosa, Brit. J. Ophth. **23**:332, 1939.

5. Brown, W. M.: Treatment of Retinitis Pigmentosa with Retrobulbar Injections of Atropine Sulfate, Arch. Ophth. **25**:819 (May) 1941.

6. Meighan, S. S.: Treatment of Retinitis Pigmentosa by Cervical Sympathectomy: Preliminary Report of a Case, Tr. Ophth. Soc. U. Kingdom **51**:124, 1931.

7. Campbell, G.: Sympathectomy in a Case of Retinitis Pigmentosa, Canad. M. A. J. **26**:674, 1932.

8. MacDonald, A. E., and McKenzie, K. G.: Sympathectomy for Retinitis Pigmentosa, Arch. Ophth. **13**:362 (March) 1935.

9. Kerr, H. H.: Surgical Treatment of Retinitis Pigmentosa, Am. J. Surg. **28**:364, 1935.

which migration of pigment is limited to the periphery of the fundus are the most satisfactory for surgical treatment, the operation being contraindicated in cases in which central vision is reduced to less than 10 per cent of normal and in which fields occupy a circle with a radius of less than 10 degrees. Walsh and Sloan [10] found only slight benefit in 1 of 3 cases after sympathectomy. De Takats and Gifford [11] were even more pessimistic. They performed 11 operations on 6 patients (4 cervicodorsal and 7 superior cervical ganglionectomies), and did not find an increase in visual acuity or in the visual fields in a single case. Caeiro,[12] using complete excision of the stellate ganglion in 13 cases, found greatly increased fields and visual acuity in 4 and increases in fields and/or acuity in 4 cases.

Use of extracts of the endocrine glands in the treatment of retinitis pigmentosa have also had many advocates. Biró [6] used testicular extract (Glandubolin) and noted improvement in 1 case. He based his treatment in part on the conclusion of Wibaut [13] that the female sex glands exert a certain resistance to retinitis pigmentosa, since this disease is much more frequent in males and occurs in a milder form in females.

The fact that vitamin deficiency, particularly of vitamin A, is frequently followed by night blindness, has led to the association of pigmentary degeneration with deficiency disease. Babel [14] produced experimental pigmentary degeneration in the rabbit by injecting sodium iodate. He found that administration of synethic α-tocopherol in sufficient quantity has an effect against sodium iodate intoxication more marked on the pigmentary epithelium than on the neural elements of the retina. Once the toxic process has been initiated, however, vitamin E has no action. Josephson and Freiberger,[15] giving carotene having a vitamin A potency of 30,000 to 60,000 U. S. P. units by intramuscular injection, found improvement after one week in cases of early disease and none in cases of the more advanced stage. Finding that retinitis-pigmentosa-like lesions developed in pups fed a diet low in vitamin D and calcium,

10. Walsh, F. B., and Sloan, L.: Results of Cervical Sympathectomy in Pigmentary Degeneration of the Retina, Arch. Ophth. **20**:311 (Aug.) 1938.

11. de Takats, G., and Gifford, S. R.: Cervical Sympathectomy in Retinitis Pigmentosa, Arch. Ophth. **14**:441 (Sept.) 1935.

12. Caeiro, J. A.: Results of Stellectomy in Treatment of Pigmentary Retinitis, Arch. Ophth. **19**:378 (March) 1938.

13. Wibaut, F.: Use of the Female Hormone in Treatment of Retinitis Pigmentosa, Deutsche med. Wchnschr. **57**:1939, 1931.

14. Babel, J.: L'action de la vitamin E sur la rétinite pigmentaire expérimentale du lapin, Ophthalmologica **107**:102, 1944.

15. Josephson, E. M., and Freiberger, M.: Carotene Therapy of Retinitis Pigmentosa, Nature, London **139**:155, 1937.

Knapp [16] treated 9 patients with at least 60 drops of activated ergosterol (viosterol) daily, plus at least 1 Gm. of available calcium. He concluded that there was a decided improvement in night vision after seven weeks, with changes in the disk toward normal in 5 cases and increased width of arterioles in 3 cases.

In the last ten years Filatov and his co-workers [1] have published a series of papers embodying the concept of "tissue therapy." Briefly, the theory holds that when tissue has been removed from the body under aseptic conditions and allowed to stand six to seven days at 2 C. certain disintegration products are released. These substances act as stimulants when the tissue is implanted or its extracts are injected. The action is not organ specific.

In an early paper in English, Filatov [1a] stated that a total of 112 patients with retinitis pigmentosa were given tissue therapy and that some improvement in visual acuity, visual fields or dark adaptation was noted even in those with the most advanced disease. This improvement was said to be lasting, especially when treatment was repeated. Placental grafts, skin grafts, implantation of liver and choroid and injections of cod liver oil or aloe were used. Later, with Verbitska, Filatov [14] reported 12 cases in which intramuscular injection of cod liver oil was given. He found that these injections produced rapid improvement, effects being noted in some instances after one to two injections. Even severe chronic forms of the disease were affected. It is Filatov's belief that the cod liver oil acted not only through its vitamins but through other by-products of the liver.

In another paper,[1b] a report was made on 60 patients treated with cod liver oil. Of these, 52 showed improvement subjectively and during the functional examination. The majority showed improvement after four to ten injections of 0.5 cc. each. In the same paper, implantation of placenta and liver is discussed. Of 22 placental implants under the conjunctiva, 22 were successful. Of 6 implantations of placenta under the skin, none was successful. Of 5 implantations of preserved liver under the skin, 4 were successful.

In two final papers, Filatov [1b, c] discussed implantation of placenta and liver. In 3 cases with subcutaneous placental implantation as well as in 2 cases with preserved liver implants, he noted encouraging, although modest, improvement and cautioned that further observation was necessary to evaluation of the treatment. Filatov [1b] concluded:

> Treatment by implantation of preserved tissues and by intramuscular injection of cod liver oil, singly or in combination, is the most effective method for retinitis pigmentosa. It does not lead to cure but aids the handicapped by restoring work capacity.

16. Knapp, A. A.: Night Blindness: Improvement with Vitamin D, Including Experimental Production of Retinitis Pigmentosa and Its Treatment in Humans with Vitamin D., U. S. Nav. M. Bull. **41**:373, 1943.

Gordon [15b] treated 128 patients by the Filatov methods. Thirty-four showed some increase in visual acuity in at least one eye. Six patients showed definite improvement in light sensitivity, i. e., 0.7 to 2.0 log units. Two others showed temporary improvement of 0.5 log unit, the retinal sensitivities returning to the pretreatment values within three months.

Gordon's studies of the visual fields of his patients were inconclusive, some eyes showing decreases in the scotomas, others showing questionable enlargements and still others showing some decrease in field. His most striking "improvements" were in visual acuity, and not in the more important visual fields.

EXPERIMENTAL INVESTIGATION

We studied 47 patients with retinitis pigmentosa and 2 with retinitis punctata albescens, using the "tissue therapy" methods of Filatov and his co-workers. We endeavored to repeat their work as closely as possible, following the translations given in the *American Review of Soviet Medicine*.

The 49 patients were divided for convenience into two groups, 22 patients receiving injections of cod liver oil only and 27 patients receiving injections of cod liver oil and placental implants. Forty of the 49 patients received a preliminary treatment of three to eight injections of peanut oil U. S. P., as indicated in tables 1 and 2. The injections were given intramuscularly every three to five days, starting with 0.5 cc. and changing to 1 cc. for the final injections. These injections had a twofold purpose: (1) to reveal those patients who might react severely to intramuscular injections, and (2) to see whether there would be any change in light sensitivity of the retina after the injection of peanut oil alone.

The cod liver oil [17] was sterilized in a boiling water bath for fifteen minutes for three successive days. It was then poured into ampules and heated to 60 to 70 C. for two hours daily for three days. After intramuscular injection with the usual aseptic precautions, the site was massaged for at least two minutes. The initial dose was always 0.5 cc. and was increased in amounts of 0.5 cc. up to 2 cc. over the period of injection. Injections were spaced from three to five days apart.

The placenta used was preserved material. A small fragment was placed in a subcutaneous pocket under aseptic precautions. Sites chosen for implantation were those which would incovenience the patient least. Separate implantations were spaced from four weeks to five months apart.

METHODS OF EVALUATION OF TREATMENT

The results of injection of cod liver oil and placental implantation were checked by four criteria, applied before and after treatment: measurements of (1) light sensitivity of the retina, (2) visual acuity and (3) visual fields and notations of (4) the patient's comments on his ability to see.

Light Sensitivity.—Tests of visual acuity and visual fields, made with standard office equipment by the usual methods, need no description. Measurements of

17. Furnished in sterile form by courtesy of Wyeth, Inc., Philadelphia. The vitamin A potency was 1,000 U. S. P. units per gram, and the vitamin D potency, 100 U. S. P. units per gram.

TABLE 1.—*Data on Patients with Retinitis*

Case	Age, Years	Duration, Years	Visual Acuity		Visual Fields	
			Pretreatment	Post-Treatment *	Pretreatment	Post-Treatment
1	60	26	R 20/200 L 20/200	R 20/200 L 20/400	R 10-40° L 10-30°	R 10-40° L 10-20°
2	43	1	R 20/70 cw 20/30 — L 20/70 cw 20/30 — 1	R 20/50 cw 20/25 L 20/100 cw 20/25 —	R 15-55° L 20-55°	R 20-60° L 20-60°
3	52	36	R 20/200 cw 20/40 L 20/200 cw 20/40 — 1	R 20/50 cw 20/30 + + L 20 + 200 cw 20/50	R 5° L 6°	5° O. U.
4	45	11	R 20/400 L 20/400	R 20/400 L 20/400	Unobtainable	Unobtainable
5	21	Since childhood	20/25 O. U.	R 20/25 — cw 20/30 — L 20/25 — cw 20/20 —	None	5° O. U.
7	32	Teens	R 20/400 cw 20/80 L 20/400 cw 20/200	R 20/200 cw 20/70 L 20/200 cw 20/40 +	2° O. U. Central scotoma for green	1-2° O. U. No central scotoma
8	40	Many years	R 20/25 L 20/25 +	20/20 — O. U.	40-60° O. U. Several paracentral scotomas, O. U.	40-60° O. U. Several paracentral scotomas, O. U.
9	27	Since infancy	R 20/200 cw 20/40 — — L 20/70 cw 20/40 —	R 20/200 cw 20/30 — — L 20/60 cw 20/40 +	R 8° L 5°	8° O. U.
13	72	Many years	Light projection O. U.	Acuity not taken	Not taken	Not taken
18	34	Not obtainable	R 20/100 + cw 20/30 L 20/40 — cw 20/30 +	R Vcw 20/70 L Vcw 20/40	Not taken	Not taken
19	56	10 or 11	R 20/50 + cw 20/30 + L 20/40 cw 20/40	R Vcw 20/50 — L Vcw 20/40 —	8° O. U.	8° O. U.
31	21	6	R 6/200 cw 10/200 L 8/200 cw 12/200	R 7/200 cw 14/200 L 7/200 cw 14/200	R 20° L 10-20°	R 10-40° L 10-40°
36	37	Approximately 5	R 20/30 — cw 20/20 — L 20/30 — cw 20/20 —	R 20/30 — } No Vcw L 20/30 + }	R 15-55° L 15-30°	R 10-30° L 10-15°
38	60	Since early childhood	20/400 O. U.	Acuity not obtained	Could not be determined accurately	Could not be determined accurately
39	38	9+	20/60 O. U.	Not obtained	Not obtainable	Not obtainable
43	29.5	Not obtained	20/30 O. U. cw 20/25 O. U.	20/30 O. U. cw 20/25	15-30° O. U.	R 15-55° L 15-30° Scotomas in newly acquired areas in both fields
44	40	Not obtained	R 20/40 L 20/40 +	Vcw 20/30 O. U.	10-15° O. U.	10-30° O. U.
45	44	Not obtained	R Vcw 20/50 L Vcw 20/40 — 1	R 20/40 — 1 L 20/70	8° O. U.	5° O. U.
46	30	Not obtained	20/100 O. U.	20/100 O. U.	Not improved	Not improved
47	30	24+	R 20/200 Vcw 20/60 + L 2/200 Vcw 20/400	R Vcw 20/40 + + L Vcw 6/200	8° O. U.	Not taken
48	22	12	R 4/200 Vcw 20/200 L 4/200 Vcw 20/200	Slight improvement	5° O. U.	Not taken
49	37	17	R 20/40 + Vcw 20/30 + + + L 20/30 — Vcw 20/25	Not determined	3° O. U.	Not taken

* Values following cw indicate visual acuity with correction.

Pigmentosa Receiving Injections of Cod Liver Oil

Treatment	Largest Changes in Post-Treatment Sensitivity, Log Units		Comment
7 injections of peanut oil 30 injections of cod liver oil	R +0.1, −0.6 L +0.2, −0.4		Consanguinity; hemophilia? Pain, redness, swelling of left arm after 23d injection of cod liver oil
7 injections of peanut oil 30 injections of cod liver oil	R +0.1, −0.1 L −0.7		No consanguinity; patient says that he and mother are bleeders
3 injections of peanut oil 30 injections of cod liver oil	R +0.6 L +0.9		No consanguinity; mother's uncle has retinitis pigmentosa
3 injections of peanut oil 30 injections of cod liver oil	Sensitivity for right eye could not be measured L +0.4, −0.4		No consanguinity; paternal grandmother, one brother of father and an older sister have retinitis pigmentosa; poor hearing for four years; large number of pigmented moles and warts on body; left arm painful, red and swollen after 28th injection of cod liver oil
6 injections of peanut oil 22 injections of cod liver oil	R +0.4 L +0.4		No consanguinity
2 injections of peanut oil 30 injections of cod liver oil	R +0.1, −0.2 L +0.2, −0.1		No consanguinity; younger brother has retinitis pigmentosa
5 injections of peanut oil 26 injections of cod liver oil			No consanguinity; severe swelling of left arm after 18th injection
31 injections of cod liver oil	R +0.1, −0.1 L +0.1, −0.1		No consanguinity; night blindness in family for several generations; retinitis punctata albescens
6 injections of peanut oil 10 injections of cod liver oil			Course of treatment not completed
3 injections of peanut oil 27 injections of cod liver oil			No consanguinity; patient deaf-mute since birth
7 injections of peanut oil 28 injections of cod liver oil	R +0.3, −0.1 L +0.3, −0.3		No consanguinity; hearing diminished
4 injections of peanut oil 30 injections of cod liver oil	R +0.1, −0.1 L +0.1, −0.1		Father and mother first cousins; sister has retinitis pigmentosa
30 injections of cod liver oil			No consanguinity
5 injections of peanut oil 30 injections of cod liver oil	R +0.4 L +0.4, −0.2		Two sisters have "eye trouble"; no consanguinity
3 injections of peanut oil 30 injections of cod liver oil	R +0.1, −0.2 L +0.2, −0.1		Parents first cousins; second child has retinitis pigmentosa and congenital cataracts; one brother and one sister have retinitis pigmentosa
12 injections of cod liver oil			Subjective improvement; more assurance; patient does not bump into objects as before treatment
30 injections of cod liver oil	R +0.4, −0.3 L +0.6, −0.7	Feb. 7- Sept. 8, 1948	Patient subjectively better; gets around better at night; is less disturbed by bright lights
30 injections of cod liver oil	R +0.4, −0.3 L Poor fixation	Feb. 7- Oct. 9, 1948	No change
30 injections of cod liver oil			Typical retinitis pigmentosa, associated with involvement of central nervous system and macular involvement; vertical nystagmus
8 injections of peanut oil 15 injections of cod liver oil	R +0.1, −0.1 L +0.1, −0.1	Nov. 14- Dec. 3, 1948	
8 injections of peanut oil 15 injections of cod liver oil	R +0.1, −0.1 L +0.1, −0.1	Aug. 6- Oct. 20, 1948	
4 injections of peanut oil 6 injections of cod liver oil	R +0.1, −0.1 L +0.1, −0.1	Oct. 14- Nov. 20, 1948	No consanguinity; patient reacted to cod liver oil injections with severe pain in buttock and unable to continue treatment

TABLE 2.—*Data on Patients with Retinitis Pigmentosa*

Case	Age, Years	Duration, Years	Visual Acuity		Visual Fields	
			Pretreatment	Post-Treatment	Pretreatment	Post-Treatment
8	26	Since childhood	20/25 O. U.	20/20 — — O. U.	R 15° L 10°	R 20-40° L 10-20° (after cod liver oil)
10	21	15	R 20/50 — — L 20/40 + +	20/40 + O. U.	5° O. U.	None taken
11	40	12	R 20/200 L C. F.°	R 5/200 L 5/200	R 10-30° Ring scotoma 15° L 30-40° Ring scotoma extending from 10-20°	None taken
12	25	Since childhood	R 20/80 cw 20/60 L 20/200 cw 20/60	R 20/70 cw 20/50 L 20/150 cw 20/60	R 10 L 9	R 8-10° L 5-6°
13	16	Approximately 10	R 20/80 Vcw 20/60 L 20/200 cw 20/200	R Vcw 20/50 + L Vcw 20/80 —	1-2° O. U.	None taken
14	28	6+	R 20/50 cw 20/25 — L 20/40 — — cw 20/20 — —	R Vcw 20/25 — L Vcw 20/70 — —	R 20-75° L 15-30°	R 20-30° L 20°
15	28	3+	R 20/25 — L 20/30 —	20/20 — — O. U.	R Ring scotoma from 15-35° L Ring scotoma from 10-40°	R Ring scotoma from 15-35° L Ring scotoma from 10-40°
16	44	7-8	20/200 O. U.	R 20/60 L 20/200	8° O. U.	None taken
17	54	15	R 20/400 L 20/40	R 20/400 L 20/40	None taken	R Field not obtainable, absolute central scotoma L 2°
18	30	Since childhood	R 5/200 cw 17/200 L 5/200 cw 1/200	R Vcw 6/200 L Vcw 1/200	5° O. U. Central scotoma for all colors except green, O. U.	None taken
20	48	31	C. F., O.U.°	Not taken	Could not be obtained	Could not be obtained
21	26	Since early childhood	R 20/60 cw 20/25 L 20/70 cw 20/30 + +	R Vcw 20/25 — L Vcw 20/25 —	Not taken	10° O. U.
22	30	20	R Vcw 20/200 + L Vcw 20/200 +	Not taken	R Ring scotoma 15-35° L Ring scotoma between 30-45° plus several islands	Not taken
24	19	17.5	R 5/200 L 4/200	R 5/200 L 4/200	Not taken	Not taken
25	47	3-4	R 20/200 L 20/100	R 20/100 L 20/70	Not taken	Not taken
26	43	30+	R 20/200 L 20/200	Not taken	7° O. U. Central color scotoma for all colors	10° O. U. Absolute central scotoma
27	37	Since childhood	20/40 O. U.	R 20/40 — — L 20/30 — — (after cod liver oil)	R 8-10° L 6-15°	R 8-10° L 10°
28	39	3-4	R 20/70 — 1 cw 20/25 L 20/30 — 1 cw 20/25 — 1	R 20/30 cw 20/25 + L 20/30 cw 20/20 — —	R 5-15° L 10°	R 15-20° L 20°
30	40	17	R 20/40 cw 20/40 + L 20/30 cw 20/30	R 20/40 + + L 20/30	5° O. U. Temporal visual islands O. U.	5° O. U.
31	19	6+	R 20/400 cw 20/30 — L 20/200 cw 20/20 — —	R Vcw 20/30 L Vcw 20/25 — —	R 8-25° L 8-15°	8-6° O. U.
33	36	15+	R 5/200 cw 20/25 L 5/200 cw 20/25	R 20/20 L 20/25 — —	8-6° O. U.	8-6° O. U.
34	19	9	R 20/50 cw 20/30 — L 20/30 cw 20/80 —	None	R 12-22° L 10-12°	R 12-22° L 10-12°
35	25	7-8	R 5/200 cw 20/200 L 20/200 cw 20/80 —	R 20/80 + L 20/70	10° O. U.	10° O. U.
37	46	Since childhood	R 6/200 cw 14/200 L 8/200 cw 14/200	R 6/200 L 5/200	8-10° O. U.	R 8° L 8-10°
40	28	10	R light projection L 20/60 Vcw R 7/200 L 20/30	R 20/400 cw 20/200 L 20/40 cw 20/40 +	None taken	None taken
41	37	8	R 20/400 L 20/400	R 20/200 L 20/200	None taken	R 8° L 8°
42	54	6	R 20/400 L 20/400	R 20/400 L 20/400	Could not be taken accurately	Could not be taken accurately

° Counting fingers at 1 foot (30 cm.).

Treatment	Largest Changes in Post-Treatment Sensitivity, Log Units	Comment
3 injections of peanut oil 30 injections of cod liver oil 2 placental implants	R —1.0 L —1.1	No consanguinity; younger brother questionable retinitis pigmentosa; after cod liver oil patient stumbled less and recognized people more easily; after placenta implantation eyes felt more relaxed and vision better in dark
4 injections of peanut oil 30 injections of cod liver oil 2 placental implants	No pretreatment test	No consanguinity; arrested tuberculosis of lungs
6 injections of peanut oil 33 injections of cod liver oil 2 placental implants	Measurement unreliable because of difficult fixation	Retinitis punctata albescens; hemorrhage in eye 4 years before beginning of treatment; cause unknown
6 injections of peanut oil 29 injections of cod liver oil 2 placental implants	No post-treatment test	No consanguinity; uncle has retinitis pigmentosa; patient felt that visual field was larger after treatment
6 injections of peanut oil 31 injections of cod liver oil 2 placental implants	R +0.2, —0.1 L —0.1, +0.2	No consanguinity; poor color perception
5 injections of peanut oil 30 injections of cod liver oil 2 placental implants	R +0.6, —0.4 } during treat- L +0.7, —0.5 } ment 1½ mo. R + 0.7; L + 0.7, —0.7	No consanguinity
5 injections of peanut oil 37 injections of cod liver oil 4 placental implants	R +0.3, —0.3 } during L +0.3, —0.2 } treatment R +0.3, —0.3 L +0.4, —0.3	No consanguinity; 3 mm. object used in field tests; vision better in dark
30 injections of cod liver oil 2 placental implants	Inadequate fixation for reliable measurements	Old macular choroiditis O. U.; hypertensive state; after treatment patient able to drive cab during day and read newspaper type plainly; preretinal hemorrhage in course of treatment in left eye
6 injections of peanut oil 22 injections of cod liver oil 1 placental implant		Father and mother first cousins; sister and mother have "eye trouble"
3 injections of peanut oil 31 injections of cod liver oil 2 placental implants	During treatment R +0.3 L +0.3	No consanguinity; father, grandfather, two brothers and sister have night blindness
27 injections of cod liver oil 1 placental implant 37 injections of cod liver oil 3 placental implants	R +0.1, —0.1 L +0.1, —0.1 R +0.2, —0.1 L +0.2, —0.4	No consanguinity; mother and two brothers have "eye trouble" No consanguinity; brother has retinitis pigmentosa; patient is subjectively improved, has side vision and larger visual range; night blindness not improved
6 injections of peanut oil 63 injections of cod liver oil 3 placental implants	No post-treatment measurements	High hypermetropia (OD:16.00 D.; OS:14.75 D.); microphthalmos; one reaction to cod liver oil midway in treatment; subjective improvement in night vision
6 injections of peanut oil 27 injections of cod liver oil 2 placental implants		Previous stellate ganglion block not successful
7 injections of peanut oil 29 injections of cod liver oil 2 placental implants	No post-treatment measurements	Father and mother first cousins
4 injections of peanut oil 29 injections of cod liver oil 1 placental implant	No post-treatment measurements	No consanguinity
3 injections of peanut oil 30 injections of cod liver oil 1 placental implant	R +0.1, —0.1 L +0.2, —0.2	No consanguinity; brother has retinitis pigmentosa; hearing poor; one reaction to cod liver oil; painful, swollen left arm
3 injections of peanut oil 30 injections of cod liver oil 2 placental implants	R +0.2, —0.2 L +0.1, —0.1	No consanguinity; younger brother has retinitis pigmentosa; marked diminution of hearing; subjective enlargements of visual field
42 injections of cod liver oil 3 placental implants	R +0.1,—0.1 L +0.1, —0.1	Exotropia; subjective improvement in color perception and ocular fatigue
3 injections of peanut oil 24 injections of cod liver oil 2 placental implants	No post treatment measurements	
3 injections of peanut oil 24 injections of cod liver oil 1 placental implant	R +0.7 L +0.4	No consanguinity; brother has retinitis pigmentosa
2 injections of peanut oil 31 injections of cod liver oil 1 placental implant	R +1.0 L +0.7	Consanguinity (?)
41 injections of cod liver oil 1 placental implant 4 injections of peanut oil 30 injections of cod liver oil 1 placental implant	R +0.4, —0.4 L +0.2, —0.5 R —0.6 L Not measured after treatment	Father and mother first cousins; brother has retinitis pigmentosa No consanguinity; 1 of 5 sisters has retinitis pigmentosa
4 injections of peanut oil 30 injections of cod liver oil 2 placental implants	R Poor fixation L —0.8	No consanguinity; sister has retinitis pigmentosa
6 injections of peanut oil 29 injections of cod liver oil 4 placental implants	R +0.1, —0.1 L +0.1, —0.1	No consanguinity; sister has retinitis pigmentosa
6 injections of peanut oil 27 injections of cod liver oil 2 placental implants		No history

retinal sensitivity, however, being in the developmental stage, require specification.[18] The apparatus and conditions, although not the basic principles, necessarily differ among the several laboratories (Hecht, Haig and Wald [19]; Crozier and Holway [20]; Sloan [21]; Mandelbaum [22]; Haig and Haig [23]) engaged in developing the technic.

A modified Hecht-Shlaer [24] dark adaptometer was employed having a fixation light tract and rider especially designed for rapid changes in the direction of fixation. The stimulus beam subtended 2 degrees of visual angle, and the duration of each test flash was 0.2 second. For most of the measurements a monochromatic yellow filter (Eastman Wratten no. 73) was used; this cut out all blue and violet light below the wavelength of 555 millimicrons, thus avoiding differential absorption of the shorter wavelengths by the yellow macular pigment. This source of error in comparing the function of one region of the retina with that of another was discussed by Wald [25] and by Haig and Haig.[23]

After a half-hour in complete darkness, the patient was instructed to fixate on the dim fixation light and to respond by saying "yes" when the test flash was seen. The intensity was varied in acccordance with these responses, and the intensity which was seen nine times out of ten was taken as the threshold. The threshold was expressed in brightness units, or lamberts (1 lambert equals 1 lumen per square centimeter), the sensitivity being the reciprocal of the threshold. The use of logarithms compresses the enormous range involved into manageable magnitudes. Daily, weekly or monthly variations rarely exceed 0.3 log unit. In general, a variation of 0.5 log unit may be regarded as significant, as it is highly improbable that such a change is attributable to an error in measurement. In evaluation of the effect of treatment on retinal sensitivity, changes in log sensitivity of 0.5 log unit or greater at any single locus, e. g., 2 or 10 degrees, were considered significant.

Measurements of sensitivity were made at the center and in the horizontal meridian as far into the periphery as possible, usually at the following loci on both sides of the fovea: 2, 4, 6, 10, 14 and 18 degrees. Normally, the sensitivity rises sharply from 2 to 6 degrees, beyond which there is little further increase.[26] In severe retinitis pigmentosa there is a steady decrease in sensitivity from 2 degrees

18. We were unable to discover how these measurements were made by Filatov and associates. However, their manner of reporting changes in light sensitivity suggests that they determined the densest neutral tint filter through which the patient could barely see a constant light source, no attempt being made to control exposure time, direction or size of stimulus.

19. Hecht, S.; Haig, C., and Wald, G.: Dark Adaptation of Retinal Fields of Different Size and Location, J. Gen. Physiol. **19**:321, 1935.

20. Crozier, W. J., and Holway, H.: The Theory and Measurement of Visual Measurements, J. Gen. Physiol. **22**:341, 1939.

21. Sloan, L. L.: Instruments and Technics for the Clinical Testing of Light Sense, Arch. Ophth. **22**:233 (June) 1939.

22. Mandelbaum, J.: Dark Adaptation, Arch. Ophth. **26**:203 (Aug.) 1941.

23. Haig, C., and Haig, E. M.: Retinal Sensitivity Contours: Abstracts of Communications, 17th International Physiological Congress, Oxford, 1947, p. 233.

24. Hecht, S., and Shlaer, S.: An Adaptometer for Measuring Human Dark Adaptation, J. Optic Soc. America **28**:269, 1938.

25. Wald, G.: Human Vision and the Spectrum, Science **101**:653, 1945.

26. Crozier and Holway.[20] Haig and Haig.[23] Hecht, Haig and Wald.[19] Mandelbaum.[22] Sloan. [21]

out as far as measurements can be made.[27] For the 20 normal subjects used in the present study, the spread of the data was 1 log unit. We may thus define as normal all values within 0.5 log unit (or 32 per cent) of the average normal.

Visual Acuity.—Some patients received a change of glasses during the treatment, the new refraction differing from the original glasses at the start of the treatment. This may account in certain cases for part of the increase in visual acuity found after treatment. In the majority of such cases, however, an accurate appraisal of the visual acuity can be made by comparing the uncorrected vision before and after treatment.

Visual Fields.—Measurements of visual fields often presented great difficulty. This was caused in part by lack of cooperation of certain patients, and in part by the difficulty involved in charting minute fields with precision.

Patients' Comments.—Comments of the patients indicated improvement in a certain number of cases, but one may not judge success by subjective criteria which have no objective substantiation in visual acuity, visual fields or light sensitivity.

RESULTS

Responses to Injection of Cod Liver Oil.—Twenty-two patients received injections of cod liver oil only. The number of injections varied from ten to thirty-one, the majority of the patients receiving thirty injections. The results are summarized in table 1. Improvement in visual acuity was negligible. A few patients showed slight increases in visual acuity in one or both eyes after treatment, but, except in 1 case (case 44), the improvement was easily within the range of variation found on different days in the same patient. The majority of patients showed either no improvement or a decrease in visual acuity.

Visual fields likewise showed little gain in most cases, with the exception of those in case 43. Considering the variation in fields which can be obtained from day to day in the same patient even with the most painstaking care, there was no significant advance in any of the other cases.

A few statements by the patients are noted, such as, "I see better" or "I am less disturbed by bright lights"; but as these statements were not supported by the objective findings to any appreciable extent, their value is doubtful.

Responses to Injections of Cod Liver Oil and Placental Implantation.—Twenty-seven patients, comprising this group, received from twenty-two to sixty-three injections of cod liver oil and from one to four separate implants. The results are given in table 2.

As with the group receiving cod liver oil, increases in visual acuity were negligible and easily within the range of daily variation. In no

27. (*a*) Haig, C.; Haig, E. M., and Saltzman, S. L.: Brightness Threshold Contours in Retinitis Pigmentosa, Anat. Rec. **96**:23, 1946. (*b*) Haig, C., and Saltzman, S. L.: Sensitivity Contours in Retinitis Pigmentosa: I. Sensitivity to White Light, Federation Proc. **6**:119, 1947. (*c*) Mandelbaum.[22] (*d*) Sloan.[21]

single case was there a significant binocular increase in acuity. There were some decreases in visual acuity. The fields likewise showed no significant improvement in any single case. A number of the fields showed significant losses as compared with the pretreatment findings.

There was subjective improvement in a few patients, such as 15, 21, 28 and 30; but, as with the patients receiving cod liver oil, this improvement is not substantiated by the objective findings.

Changes in Light Sensitivity in Response to Either Method of Treatment.—Thirty-two patients were tested before and after treatment, as exhibited in tables 1 and 2. Twenty patients showed no significant increases or decreases in sensitivity. Eight patients (25 per cent) showed significant decreases in sensitivity at one or more loci in one or both eyes. Six patients (19 per cent) showed significant increases in sensitivity at one or more loci in one or both eyes. However, 2 of these patients, 14 and 44, also had significant decreases in sensitivity in the same eye.

For all of the measurements of light sensitvity the average maximum positive deviation (improvement) is equal to the average maximum negative deviation (regression), viz., 0.3 log unit. Indeed, for most patients the measurements were mainly remarkable for their great constancy.

COMMENT

On the whole, the results of treatment are essentially without significance, as it is well established that variations in visual functions similar to those which we observed can be obtained with no treatment whatever. It is especially significant that the percentage of decreases in retinal sensitivity is greater than the percentage of increases. The visual acuity and visual field responses are equally equivocal. Such results with 49 patients do not seem to justify extension of the series to a larger number of patients.

SUMMARY AND CONCLUSIONS

Forty-seven patients with retinitis pigmentosa and 2 patients with retinitis punctata albescens were treated with intramuscular injections of cod liver oil and intramuscular injections of cod liver oil plus subcutaneous and subconjunctival placental implants, according to the methods of Filatov and his co-workers. No significant lasting improvement was observed in visual acuity, visual fields or light sensitivitv.

USE OF PARAAMINOSALICYLIC ACID ALONE OR IN ASSOCIATION WITH STREPTOMYCIN IN OCULAR TUBERCULOSIS

Experimental and Clinical Investigations

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OF THE substances recently proposed for the chemotherapy of of tuberculosis, only sulfones and streptomycin have received attention from ophthalmologists, while information is still lacking on the most recent discovery in this field, paraaminosalicylic acid, already recognized as valuable in treatment of extraocular tuberculosis. The Tb 1/698 of Domagk (a thiosemicarbazone preparation) and the "asiaticoside" (derived by Boiteau from the plant Hydrocotyle asiatica) are still awaiting a more complete trial of their antituberculosis properties.[1]

It would take too much space to report here what has already been done with sulfones and streptomycin in experimental ocular tuberculosis, and it seems hardly necessary to recall the outstanding contributions published in the United States by Steenken and his associates, and in particular by Alan Woods and his collaborators.

They proved that sulfones (promin® [N, N'-didextrose sulfonate, the sodium salt of p,p'-diaminodiphenyl sulfone]) and promizole® [4, 2'-diaminophenyl-5'-thiazolylsulfone]) exert a definite deterrent action on the course of experimental ocular tuberculosis, especially evident in immune-allergic rabbits, as is the case with streptomycin. The effect of the combined treatment with the two drugs (streptomycin and sulfones) is somewhat greater than would be expected from a mere summation of the two substances. No sterilization of the tuberculous ocular tissues was attained, however, and only a clinical inactivation occurred. These results are in agreement with those previously obtained with streptomycin by Grigniolo, in my clinic, and by Missiroli and Monbrun and their co-workers.

Read at the Eighty-Fifth Annual Meeting of the American Ophthalmological Society, Hot Springs, Va., June 1949.

1. Some experimental investigations carried out later by me with Tb J/698 show that this drug also has a pronounced bacteriostatic effect on ocular tuberculosis, even more marked than paraaminosalicylic acid and streptomycin; it is, however, more toxic.

Much less known and less happy are the results of the clinical use of sulfones and of streptomycin (alone or associated) in cases of ocular tuberculosis. From my own experience, and from the data which I have collected from several European ophthalmologists on about 150 cases of ocular tuberculosis, it appears that sulfones are clinically of slight value, while better results are obtained with streptomycin, alone or in association with the sulfones. Streptomycin is especially effective in cases of tuberculosis of the conjunctiva and of miliary tuberculous nodules of the choroid. On the contrary, variable results were obtained in cases of the other uveal forms of the disease. The drug was often ineffective in treatment of periphlebitis retinae. One is compelled, therefore, to conclude that the therapeutic problem of ocular tuberculosis could hardly be considered as fully solved.

Moreover, some toxic effects appear, and some physicians are reluctant to give streptomycin for localized lesions lest there should develop a resistance in the tubercle bacilli, which would preclude the successful use of the drug in the future.

On the contrary, the property of producing resistance in the tubercle bacilli is not shared by paraaminosalicylic acid (2-hydroxy-4-aminobenzoic acid), the antituberculosis activity of which was discovered recently (1946) by Lehmann, of Sweden. Even in dilutions of 1:650,000 to 1:10,000,000, paraaminosalicylic acid shows a bacteriostatic activity on the tubercle bacillus, interfering with its metabolism, affecting the enzyme system or perhaps the deaminization of the amino acids.

Experimentally, paraaminosalicylic acid reduces the mortality rate of tuberculosis-infected animals and the extent of the tuberculous lesions but is generally unable to prevent the onset of the disease (Lehmann, Youmans, Feldman and associates, McClosky and associates, and others).

Paraaminosalicylic acid is well tolerated by man when administered orally and parenterally in large doses (10 to 15 Gm. daily) necessary to maintain an adequate concentration in the blood, even if vomiting and diarrhea occur. Its sodium salt, which is highly soluble, is employed also locally. It is still too early to draw definite conclusions as to the effectiveness of paraaminosalicylic acid in the treatment of general clinical tuberculosis, but there is little doubt that the compound exerts an inhibiting action on tuberculous lesions, which regress under local or general treatment. The combined administration of paraaminosalicylic acid and streptomycin seems to give better results than when the drugs are given separately.

Since no reports are as yet available on the activity of paraaminosalicylic acid on ocular tuberculosis, I was interested in investi-

gations on this subject. My associate, Brognoli, and I noted first that oral administration of paraaminosalicylic acid or injections of its sodium salt are followed by detectable passage of the drug into the aqueous of the rabbit, its rate being somewhat inferior to that of the blood (10 and 6.5 mg. per hundred cubic centimeters, respectively, one-half hour after the administration of 1 Gm. of paraaminosalicylic acid per kilogram of body weight). In the secondary aqueous or in the inflamed eye the level of paraaminosalicylic acid is very close to that of the blood. Iontophoresis (5 per cent solution of the sodium salt, with the negative pole on the eye) and, to a lesser degree, subconjunctival injections are also followed by the passage of the drug into the aqueous. Determination of the level of paraaminosalicylic acid in the body fluid was performed with the Ehrlich reagent (paradimethyl-

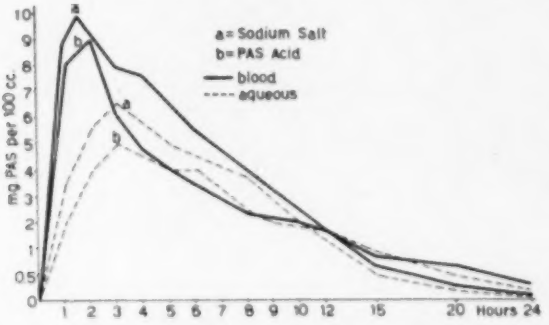

Fig. 1.—Concentrations of paraaminosalicylic acid in the blood and aqueous after oral administration of 1 Gm. of the drug per kilogram of body weight (rabbit).

aminobenzoaldehyde), which gives a yellow color with paraaminosalicylic acid, the intensity being determined with the Pulfrich graduated photometer (filter S. 43).

EXPERIMENTAL INVESTIGATIONS

Investigations on the tuberculostatic properties of paraaminosalicylic acid in the eye were performed on guinea pigs and on rabbits.

1. *First Series.*—Forty guinea pigs (average weight, 350 to 400 Gm.) were given injections into the anterior chamber of the right eye of 0.01 mg. of a six week old Sauton medium culture of virulent human tubercle bacilli. The strain was previously tested in vitro for its sensitivity to streptomycin and paraaminosalicyclic acid; both drugs proved effective. Six animals served as untreated controls; the others

were divided into three groups. To the first group, of 16 guinea pigs, 250 to 300 mg., and later (after fifteen days) 500 to 600 mg., of paraaminosalicylic acid were given twice a day; a second group, of 11 animals, was given subcutaneous injections of 50 mg. of streptomycin, divided into two daily doses, and the last group, of 7 animals, received

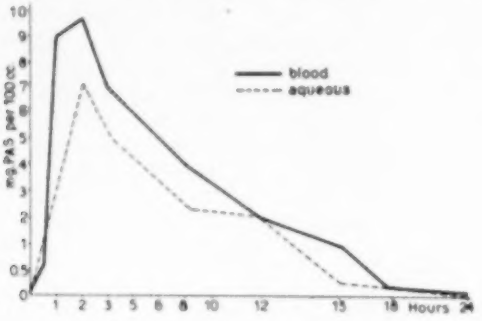

Fig. 2.—Concentrations of paraaminosalicylic acid in the blood and aqueous following intravenous injection of 1 Gm. of the sodium salt of the drug per kilogram of body weight.

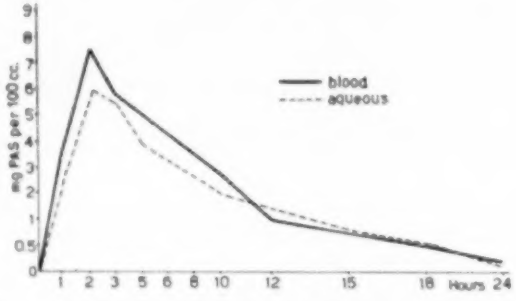

Fig. 3.—Concentrations of paraaminosalicylic acid in the blood and aqueous following intramuscular injection of 1 Gm. of the sodium salt of the drug per kilogram of body weight (rabbit).

paraaminosalicylic acid and streptomycin in the aforementioned doses. The treatment began twenty-four hours after the inoculation of tubercle bacilli and was continued for seventy-five days. The drugs were well tolerated and no toxic manifestations were recorded, except for a rather stationary growth curve as compared with that for the controls.

In the untreated animals, typical tuberculosis of the iris appeared on the tenth to the twelfth day after inoculation, to be followed soon by clouding of the cornea and enlargement of the eyeball, with corneal perforation between the twenty-second and the twenty-fifth day.

In the guinea pigs fed paraaminosalicylic acid, the tubercles of the iris became evident on the nineteenth day after the infection; and, even if the drug did not arrest the progress of the disease, the course was

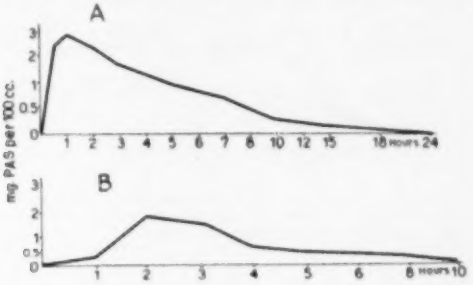

Fig. 4.—*A*, concentration of paraaminosalicylic acid in the aqueous following iontophoresis of the cornea (rabbit) with a 5 per cent solution of the sodium salt of the drug. *B*, concentration of paraaminosalicylic acid in the aqueous following subconjunctival injection of 1 cc. of a 50 per cent solution of the sodium salt of the drug in the rabbit.

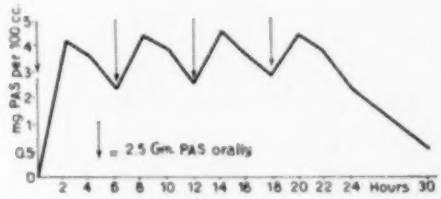

Fig. 5.—Blood levels of paraaminosalicylic acid in man following repeated oral administration (2.5 Gm. every six hours).

much milder and in no instance did a corneal perforation occur during the period of administration of the paraaminosalicylic acid.

In the animals treated with streptomycin alone the lesion of the iris became evident on the twenty-first day, and the course of the disease in the following days was milder than in the control animals and in those fed paraaminosalicylic acid. The disease was generally arrested at the stage of formation of the iris nodules, without corneal involvement or enlargement of the bulbus. No regression of the nodules could,

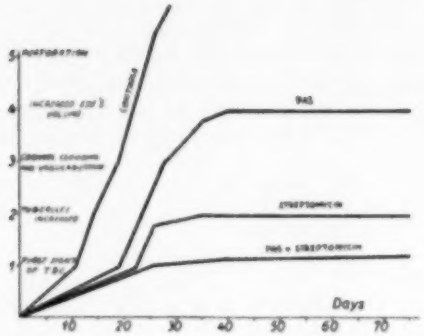

Fig. 6.—Graph showing the course of the tuberculous infection in guinea pigs treated with paraaminosalicylic acid and streptomycin (alone or associated) twenty-four hours after inoculation of the anterior chamber.

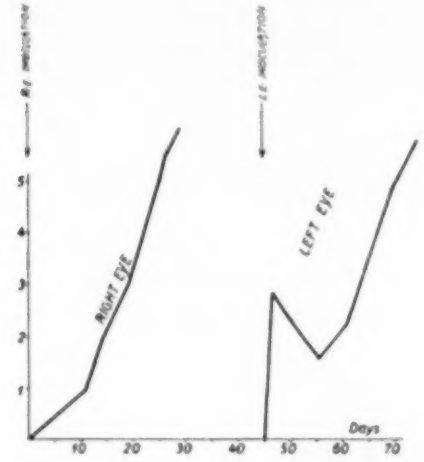

Fig. 7.—Course of tuberculosis in untreated controls (guinea pigs of figure 6) in the first and in the second inoculated eye. Except for the allergic reaction just after the inoculation of the second (left) eye, the course of the disease is practically identical in the two eyes.

however, be recorded, notwithstanding the uninterrupted administration of the antibiotic.

In the animals treated with a combination of paraaminosalicylic acid and streptomycin, the onset of the disease was delayed, at least after the twenty-fifth day, and in 3 cases iris tubercles failed to develop even seventy-five days after the inoculation. The course of the disease in this group was definitely milder than in the previous groups.

After seventy-five days the treatment was discontinued. For about ten days no changes occurred in the aspect of the eye. Later the disease progressed also in the animals which until that moment had

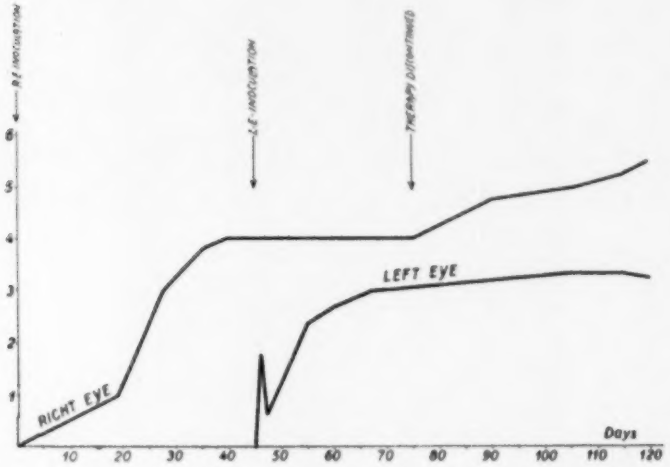

Fig. 8.—Course of the disease in guinea pigs (fig. 6) treated with paraaminosalicylic acid. In the second (left) inoculated eye, in addition to the allergic reaction, it is to be noted that the disease displays a milder course than that in the first infected (right) eye and remains nearly stationary even when the therapy is discontinued, while tuberculosis progresses in the first eye.

shown apparently normal eyes. Cutaneous tests with tuberculin performed forty-five days after the appearance of the infection elicited responses more or less proportional to the intensity of the ocular lesions.

2. *Second Series.*—At the time of the tuberculin tests a reinfection of the hitherto untouched (left) eye was produced with the same technic as that employed for the right eye. Within forty-eight hours the eye manifested an intense allergic reaction, more or less proportional to the intensity of the disease in the right eye. The reaction subsided very slowly in the succeeding days and later became

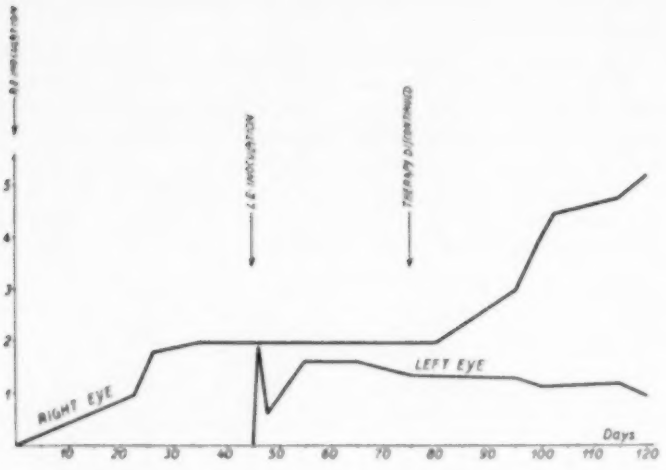

Fig. 9.—Course of the disease in guinea pigs (fig. 6) treated with streptomycin.

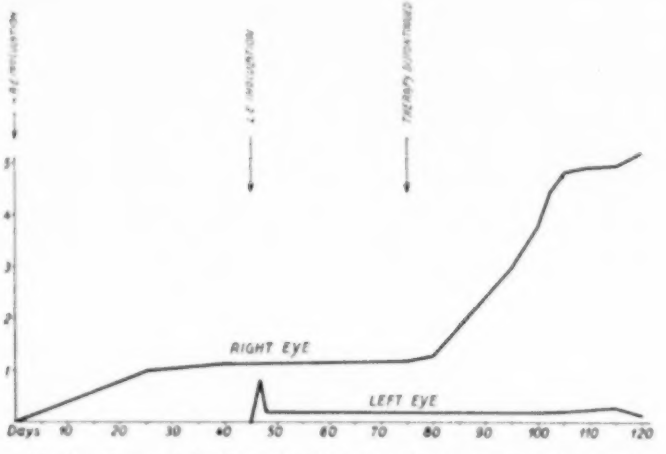

Fig. 10.—Course of the disease in guinea pigs (fig. 6)) treated with paraamino-salicylic acid and streptomycin. The same phenomena, more pronounced than in figures 8 and 9, are observed.

associated in the controls with the typical tuberculous process. The disease in the second eye of these highly allergic animals (untreated controls) was severer than in the first eye. As was expected, the allergic phase was unaffected by paraaminosalicylic acid and streptomycin therapy. On the contrary, these two substances, especially if associated, acted on the course of the disease in the second (left) eye better than in the first one.

When the therapy was discontinued (seventy-five days after the inoculation in the right eye and thirty days after that in the left eye) the disease, although it had progressed in the first eye, being incompletely

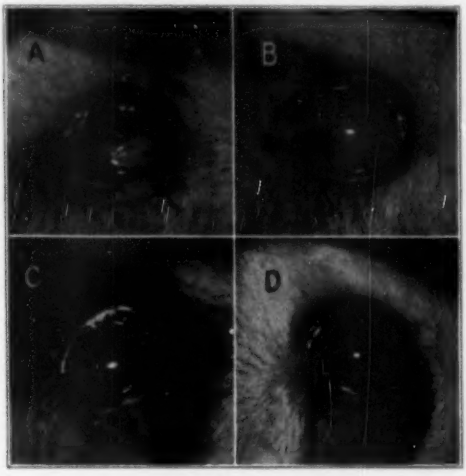

Fig. 11.—Guinea pig eyes thirty days after infection (see figure 6). *A*, untreated eye; *B*, eye treated with paraaminosalicylic acid; *C*, eye treated with streptomycin; *D*, eye treated with paraaminosalicylic acid and streptomycin.

controlled, had remained stationary in the second eye and cicatrization followed.

From these results, one may assume that after the first inoculation an immunoallergic condition developed, a condition which acted favorably on the course of the disease, enhancing the effects of paraaminosalicylic acid and streptomycin.

3. Third Series.—I later performed experiments on guinea pigs and on rabbits to discover whether paraaminosalicylic acid alone or in association with streptomycin was able to exert a therapeutic effect on the disease when already established. For that purpose 32 already

immune-allergic animals (16 guinea pigs and 16 rabbits) were used, according to the suggestion of Alan Woods. An infection with tubercle bacilli (0.01 mg.) of the same strain as that used in the previous experiments was produced in the right eye of the animals. An allergic-tuberculous reaction developed after twenty-four hours and rapidly subsided.

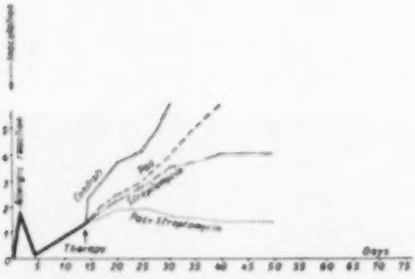

Fig. 12.—Graph showing course of tuberculous infection in immune-allergic guinea pigs treated with paraaminosalicylic acid and streptomycin (alone or associated) when the disease was already established.

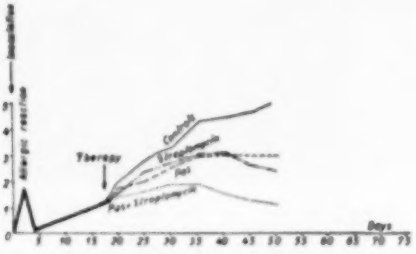

Fig. 13.—Graph showing course of tuberculous infection in immune-allergic rabbits treated with paraaminosalicylic acid and with streptomycin (alone or associated) when the disease was already established.

Iris tubercles began to appear in eleven to sixteen days. The animals were then divided into four groups. The first group served as the untreated control; the second received 1 (rabbit) to 2 (guinea pig) Gm. of paraaminosalicylic acid per kilogram of body weight orally each day; the third was given 100 to 50 mg. of streptomycin subcutaneously, and to the fourth the two drugs were jointly administered. The treatment began on the fourteenth day in guinea pigs and on the eighteenth day in rabbits.

In the untreated animals the disease showed a severe, rapidly progressive course, which ended in perforation of the cornea. In the guinea pigs fed paraaminosalicylic acid, the course of the disease was milder than in the untreated controls, but the drug did not prevent the

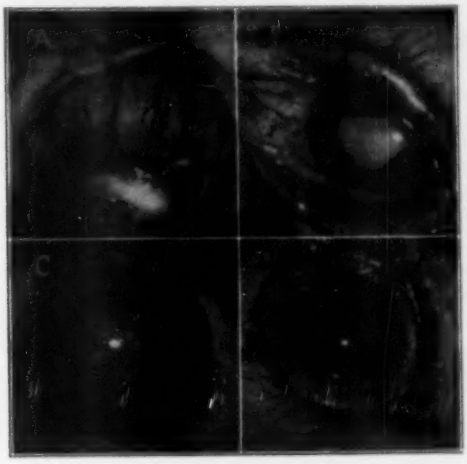

Fig. 14.—Rabbit eyes forty days after infection (see figure 13). *A*, untreated eye; *B*, eye treated with paraaminosalicylic acid (treatment begun twenty days after infection); *C*, eye treated with streptomycin; *D*, eye treated with streptomycin and paraaminosalicylic acid.

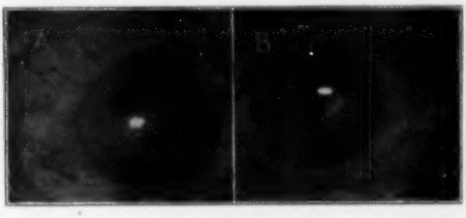

Fig. 15.—Corneal tuberculosis in human eye (case 1) before and after treatment with paraaminosalicylic acid.

enlargement of the bulbus, with subsequent perforation, which occurred about seven to ten days later than in the controls. Similar results were observed in rabbits, in which, however, the disease was not so severe and did not reach the stage of perforation.

Quite similar were the results obtained in the streptomycin-treated group, although the drug was more effective than paraaminosalicylic acid in these animals.

Undoubtedly the most brilliant results were recorded in those receiving both paraaminosalicylic acid and streptomycin; after a first period of progression the disease was arrested; later, especially in guinea pigs, it regressed, evolving slowly toward cicatrization.

Comment.—All these experiments prove that in the eye, too, paraaminosalicylic acid exerts a tuberculostatic effect, which, unlike the action of sulfones, according to Woods and Burky, is evident also in non-immune-allergic animals; in these animals, the substance, however, is more effective. Even if paraaminosalicylic acid (at least in the doses employed, which are four to eight times as high as those employed for human subjects, since the animals are more sensitive to tuberculosis) seems inferior to streptomycin, the association of the two drugs gives a more intense effect than their use separately. Nevertheless, the substances did not, at least in the doses administered and in the kind of infection produced, inhibit definitely the onset of the disease in the majority of animals even when preventively administered; the disease, however, showed a much milder course and was arrested by the therapy. The effects were more pronounced in immune-allergic animals, in which, notwithstanding the relatively short period of treatment (thirty days), the infection remained stationary or regressed when the therapy was discontinued. The disease progressed, on the contrary, in the first eye (infected when the animal was normal, not allergic) when the therapy, after seventy-five days, was interrupted.

CLINICAL INVESTIGATIONS

Our experimental investigations were soon followed by clinical trials of paraaminosalicylic acid in treatment of human ocular tuberculosis.[2] Eighteen patients have thus far been treated by me and by several Italian ophthalmologists, who gave me personal reports on their cases. My patients received 10 to 12 Gm. of paraaminosalicylic acid daily (divided in four doses) for a twenty day course, and the course was repeated once or more times, sometimes in association with 0.5 to 1 Gm. of streptomycin. When paraaminosalicylic acid was not well tolerated, its sodium salt was given, still orally or by injection. In 3 patients iontophoresis three times a day with a 5 per cent solution of the sodium salt was also carried out.

The administration of 2.5 to 3.5 Gm. of paraaminosalicylic acid every six hours permits the maintenance of a blood level of 3.5 to 5 mg.

2. For the criteria followed in the diagnosis of ocular tuberculosis, see Mistroli, G.: Boll. d'ocul. **26**:31, 43 and 171, 1947. Pasca, G.: ibid. **27**:439, 1948.

Data on Patients with Ocular Tuberculosis Treated by Paraaminosalicylic Acid Alone or with Streptomycin

Patient No.	Sex	Age	Diagnosis	Therapy Performed	Results
1	F	20	Corneal tuberculosis, right	10 Gm. PAS daily for 20 days; course repeated; iontophoresis with sodium salt of PAS	Cure in 2 months; vision 6/10; previous unsuccessful treatment with streptomycin
2	F	25	Corneal tuberculosis, right	10 Gm. PAS daily for 20 days (three courses); iontophoresis with sodium salt of PAS	Cure in 2 months; vision 3/10
3	F	26	Diffuse severe uveitis, left (eye subatrophic)	10 Gm. of PAS daily for 20 days (course repeated)	Already subatrophic eye quiet in 2½ months
4	F	29	Disseminated choroiditis, left	10 Gm. PAS daily for 20 days; course repeated; 0.50 Gm. streptomycin daily for 20 days	Slight improvement during first month of therapy; eye healed in 3 months
5	M	52	Anterior uveitis with anterior chamber tubercle and sec. corneal involvement	10 Gm. PAS daily for 20 days; course repeated; iontophoresis	Rapid improvement during first month of therapy; cure in 2 months, with large scars and synechiae
6	F	38	Nodular iritis after iridectomy for pupillary occlusion R.; cataract	10 Gm. PAS (sodium salt, partly intravenously) daily for 25 days; course repeated three times	Nodules disappeared after the second course; eye quiet after third course
7	F	21	Total uveitis, right	10 Gm. PAS daily for 10 days; course repeated twice; administration of roentgen rays, ascorbic acid and calcium (treated by Sabbadini)	Vision from 2/10 to 7/10; keratitis punctata disappeared; vitreous nearly clear; condition later stationary
8	M	45	Anterior not severe uveitis, right	10 Gm. PAS daily for 10 days; use of roentgen rays, ascorbic acid and calcium (therapy irregular)	Vision from 7/10 to 9/10; keratic precipitates reduced; vitreous clearer; later, condition worse
9	M	27	Disseminated choroiditis, right; tuberculosis of lung	10 Gm. daily for 10 days; course repeated thrice (treated by Gandolfi)	Vision from 1/10 to 4/10; regression and pigmentation of fundus lesions
10	M	50	Periphlebitis retinae; choroidoretinitis juxtamacularis (right) eye	10 Gm. daily for 2 days, then 5 Gm. for 2 days; after 4 days interval course continued with same scheme for 1 month; two months later 10 Gm. daily for 20 days (treated by Valerio)	Reduction of retinal hemorrhages; no further benefit from third course; drug badly tolerated
11	M	..	Exudative choroidoretinitis with slight signs of retinal periphlebitis	10 Gm. PAS daily for 20 days; course repeated twice (treated by Galeazzi)	Objective and subjective improvement after first course of PAS therapy
12	M	20	Tuberculoma of the ciliary body and choroid (right)	12 Gm. PAS daily for 20 days, 0.5 Gm. of streptomycin daily; course repeated twice	Clinical picture unchanged
13	F	17	Papilloretinitis (right) in a highly allergic patient	8 Gm. PAS (sodium salt) for 20 days	(Previous therapy ineffective) Rapid improvement with PAS; vision from 4/10 to 8/10
14	F	14½	Superficial infiltration, nodular keratitis (left)	10 Gm. PAS daily for 7 days, then for 8 days (previous unsuccessful treatment with ordinary means for 3 months) (treated by Raverdino)	Cured; vision 10/10
15	F	28	Iridocyclitis with keratic precipitates and Tyndall's sign in the aqueous (left)	10 Gm. daily for 7 days; course repeated but not completed; vitamin D therapy; iontophoresis with PAS (treated by Raverdino)	Slight improvement
16	M	18	Retinal periphlebitis (right)	Previous ordinary treatment unsuccessful; PAS given orally not tolerated; proctoclysis of 10 Gm. PAS twice daily for 10 days; 1 Gm. streptomycin daily (treated by Raverdino)	Prompt reduction of hemorrhages

per human cubic centimeters, whereas the corresponding concentration in the aqueous is 2.5 to 4 mg. By the associated use of iontophoresis higher levels can be reached.

The results may be considered as reasonably good and as encouraging the further trial of the therapy. Moreover, the general well-being, appetite and body weight are often improved.

CONCLUSIONS

From the clinical and experimental data I have assembled, one may conclude that the combination of paraaminosalicylic acid and streptomycin undoubtedly controls, much better than the hitherto employed therapeutic agents, including the sulfones, experimental and clinical ocular tuberculosis, even if this action is often limited.

In the evaluation of the effectiveness of chemotherapy, one must not forget that ocular tuberculosis, especially the uveal type, is a complicated phenomenon, in which are present peculiar immune-allergic features that are practically unaffected by chemotherapy but that play an important part in the disease, as was clearly demonstrated by Alan Woods.

In the treatment of ocular tuberculosis, an advantage is offered in the small number of bacilli generally present and in the possibility of the maintenance of high levels of the drug in the aqueous by topical application, allowing a more intimate contact of the drug with the very core of the tuberculoma. It is particularly to be remembered that the best results, for instance with paraaminosalicylic acid, were obtained in the treatment of empyema by topical application of the chemotherapeutic agent.

I think chemotherapy, by combining the oral administration of paraaminosalicylic acid and the intramuscular injection of streptomycin, with the addition of iontophoresis for the lesions of the anterior segment of the eye, should be tried in every case of active ocular tuberculosis, in addition to the classic means of therapy, such as tuberculin (to desensitize the organism, along the lines so clearly established by Alan Woods), climatotherapy, administration of calcium and vitamins and the maintenance of good nutrition. The dose (10 to 15 Gm. of paraaminosalicylic acid and 0.5 to 1 Gm. of streptomycin given daily in three week courses, to be repeated once or more times) is intended to maintain a sufficient concentration of the drugs in the eye; thus, serious toxic manifestations are avoided, and the organism is permitted a proper defensive reaction. In effect, since in the doses used the drugs are only bacteriostatic, the killing of the tubercle bacilli and the healing of the lesions must be accomplished by the body mechanisms of immunity and defense, which should be properly augmented.

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DIBUTOLINE SULFATE

Comparative Clinical Study of Cycloplegic Effects

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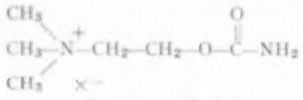
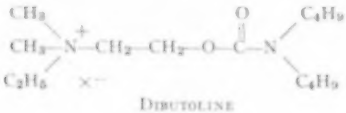
IN 1944 Swan and White[1] found that certain derivatives of a number of choline esters, rather than possessing a parasympathomimetic action comparable to other choline esters, competed physiologically with the acetylcholine normally present in the body and thus behaved as parasympatholytic drugs. The most promising member of this group appeared to be dibutylcarbamate of dimethylethyl-2-hydroxyethyl ammonium sulfate, which was given the name dibutoline sulfate.



CARBACHOL U. S. P.



DIBUTOLINE

PHARMACOLOGY

Dibutoline sulfate (dibutylcarbamate of dimethylethyl-2-hydroxyethyl ammonium sulfate) is chemically related to carbachol U. S. P. (carbamylcholine chloride; doryl®) but possesses different physical properties and has antagonistic pharmacologic effects on the intraocular muscles. For example, dibutoline is surface active and mydriatic; carbachol is surface inactive and miotic.

Dibutoline produces paresis of smooth muscles innervated by the parasympathetic nervous system. Its effect on the smooth muscles, therefore, simulates that of paralysis of the oculomotor nerve, that is,

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From the Refraction Department of the Wills Hospital.

Presented at the First Annual Wills Hospital Conference, May 6, 1949.

Dibutoline sulfate was made available by Merck & Co., Rahway, N. J.

1. Swan, K. C., and White, N. G.: Choline Esters with Atropine-like Action, J. Pharmacol. & Exper. Therap. **80**:285-288 (March) 1944.

paresis of the sphincter of the iris and the ciliary muscles. Its action on the intraocular muscles is antagonistic to that of pilocarpine, physostigmine, acetylcholine and carbamylcholine. Dibutoline has no effect on the ocular muscles innervated by the sympathetic nervous system.

The exact site of action has not yet been established. However, it probably acts directly on the muscle cells, since it reduces the reactivity of the sphincter of the iris to direct electrical stimulation, as well as to electrical stimulation of the oculomotor nerve.

CLINICAL USE

Swan and White[2] instilled a 7.5 per cent aqueous solution of dibutylcarbamate of choline sulfate in one eye and 2 drops of 5 per cent homatropine hydrobromide in the other eye of 400 patients for comparison. They found little difference in the degree of mydriasis and cycloplegia produced by the two drugs. However, the effects were less prolonged after instillation of the dibutylcarbamate of choline sulfate.

At Wills Hospital, we determined to investigate the new drug, dibutoline sulfate, and to compare its effect with that of 4 per cent homatropine hydrobromide in 1 per cent hydroxyamphetamine hydrobromide ophthalmic (1 per cent paredrine® hydrobromide ophthalmic, a 1 per cent solution of *p*-hydroxy-a-methylphenylethylamine hydrobromide in distilled water, made tear isotonic with 2 per cent boric acid preserved in merthiolate, 1:50,000), and with 4 per cent homatropine hydrobromide alone. A 5 per cent solution of dibutoline sulfate was used on the recommendation of the manufacturer. It was further decided to use the drug combined with 4 per cent homatropine hydrobromide to see whether the synergistic effect was equal to or greater than the effect of either drug alone. No studies were done on the amount of pupillary dilation because the cycloplegic effect was the one under study.

All the patients studied were from the refraction clinic of the Wills Hospital. The patients were unselected except that they were between the ages of 16 and 40 and the eyes under observation were those in which visual acuity could be improved to 6/6.

One will be impressed by the relatively large amount of residual accommodation with all the drugs. This can be understood when one considers that 40 per cent of the patients are Negroes and that the effect of cycloplegic drugs is notoriously inconsistent in members of this race. Because of this fact, it is felt that such a group constitutes an ideal source of investigation in determining cycloplegic effectivity.

2. Swan, K. C. and White, N. G.: Some New Choline Esters with Cycloplegic and Mydriatic Action, Proc. Soc. Exper. Biol. & Med. **53**:164-166 (June) 1943.

At the Wills Hospital, and in many practices, the following routine is used with patients between the ages of 16 and 40. A solution of 4 per cent homatropine hydrobromide in 1 per cent hydroxyamphetamine hydrobromide ophthalmic is used, after the method described by Tassman.[3] One drop is instilled in each eye, and the instillation is repeated in five minutes. The patient is then ready for examination in one hour after the instillation of the first drop. At the end of this time, if the cycloplegia is adequate, the cycloplegic acceptance will correspond to the retinoscopic findings.

COMPARATIVE STUDY OF AMOUNT OF RESIDUAL ACCOMMODATION

A group of 100 patients were examined by our usual method. All these subjects were between the ages of 16 and 40 and had a visual acuity of 6/6 or better. One week later the same patients were reexamined. This time a 5 per cent solution of dibutoline sulfate was used, 1 drop being instilled in each eye and the instillation repeated in

TABLE 1.—*Amount of Residual Accommodation Due to the Various Drugs*
(100 Patients; 200 Eyes for Each Drug)

Drug	Residual Accommodation, Diopters		
	Up to 1.50	1.75 to 2.25	2.50 or More
4% homatropine hydrobromide and 1% hydroxyamphetamine hydrobromide ophthalmic	33%	46%	21%
5% dibutoline sulfate	40%	38%	22%
4% homatropine hydrobromide	89%	40%	19%

five minutes. We determined the refractive error and measured the residual accommodation for all these patients. This was done after the method advised by Ludvig and described by Yasuna.[4] By residual accommodation we mean the accommodative ability of the eye remaining in the presence of the paralyzing effect of the cycloplegic. Some prefer to call this the depth of cycloplegia. However, we feel the former term is more suitable.

The residual accommodation was measured by first rendering the eye emmetropic; that is, the cycloplegic acceptance for distance was determined and placed before the eye. A card with Jaeger 1 print was placed before the eye at a distance of 33 cm. A +3.00 D. sphere was added to the trial frame. The plus sphere was then increased 0.25 D. at a time until the print blurred, and a notation was made of the total sphere, in addition to the emmetropic correction. If the

3. Tassman, I. S.: Use of Paredrine in Cycloplegia, Am. J. Ophth. **21**:1019 (Sept.) 1938.

4. Yasuna, E.: Homatropine Paredrine Emulsion, Arch. Ophth. **30**:87-91 (July) 1943.

refraction is correct, more than 3.25 D. sphere will blur this line of print. The strength of the +3.00 D. sphere was then decreased 0.25 D. at a time and a notation made of the amount of minus sphere which when added to the +3.00 D. sphere would make the test type illegible. Thus, if the line of type could be read with a +2.00 D. sphere and could still be seen with a +3.25 D. sphere, we considered that the amount of residual accommodation was 1.25 D. One may keep the test line at 50 cm. and measure the accommodation with a +2.00 D. lens. The distance used is arbitrary, and the results are similar. We selected the 33 cm. distance purely out of convenience.

From these figures one can readily see that 5 per cent dibutoline sulfate has practically the same effect on accommodation as 4 per cent homatropine hydrobromide with 1 per cent hydroxyamphetamine hydrobromide ophthalmic. The relatively high number of subjects with more than 2.50 D. of residual accommodation can be explained by the fact that a great proportion of our clinic patients are Negroes, and it has been our observation, as well as that of others, that too often cycloplegic drops are ineffective, and produce even poor mydriasis, in a high percentage of persons of the Negro race.

One hundred patients were likewise examined with 4 per cent homatropine hydrobromide used alone by the two drop method.

The results of these studies substantiated the report of Swan and White as to the comparative effects of homatropine and dibutoline when used separately.

SYNERGISTIC EFFECTS OF DIBUTOLINE SULFATE

Swan and White reported that when homatropine hydrobromide and dibutoline sulfate were injected simultaneously into the anterior chamber of the rabbit eye, dilation of the pupil was produced in doses approximately one-fourth the minimal effective dose of each drug when injected separately. They concluded, therefore, that the effects of the drugs were synergistic rather than purely additive.

We then determined to study the synergistic effect of 5 per cent dibutoline sulfate combined with 4 per cent homatropine hydrobromide. Again, the patients in this group were between the ages of 16 and 40 and had a visual acuity of 6/6 or better. The routine followed was instillation of 1 drop of 5 per cent dibutoline sulfate solution in each eye. Five minutes later 1 drop of 4 per cent homatropine hydrobromide with 1 per cent solution of hydroxyamphetamine hydrobromide ophthalmic was instilled in each eye, and the patient was examined after one hour. Thirty-five patients were examined by this method.

We then selected 35 other patients and reversed the order of administration of the drugs, using first the homatropine and hydroxyam-

phetamine solutions and then the dibutoline. This was done because Swan and White reported that a transitory punctate disturbance of the corneal epithelium of the rabbit eye was produced by dibutoline and we wished to determine whether or not this alteration of the corneal epithelium enhanced the effect of the drug. Actually, no appreciable difference in the amount of residual accommodation with either method was noted.

Finally, when the same effect was noted regardless of the order of the drug used, a solution was formed by mixing equal parts of 5 per cent dibutoline sulfate and 4 per cent homatropine hydrobromide. Thirty patients were examined with this mixture, thus giving a total of 100 patients in whom the combination of dibutoline and homatropine was used.

From these figures, it is quite apparent that the cycloplegic effect due to the synergistic action of dibutoline and homatropine is greater

TABLE 2.—*Synergistic Effect of Dibutoline and Homatropine on Residual Accommodation*
(100 Patients; 200 Eyes for Each Method)

Drug	Residual Accommodation, Diopters		
	Up to 1.50	1.75 to 2.25	2.50 or More
2.5% dibutoline sulfate and 2% homatropine hydrobromide	69%	40%	9%
4% homatropine and 1% hydroxyamphetamine hydrobromide opthalmic	33%	49%	22%
4% homatropine hydrobromide	35%	46%	19%
5% dibutoline sulfate	40%	39%	23%

than the effect of either drug alone (table 2). This corroborates clinically what Swan and White observed in their laboratory animals.

A residual accommodation of more than 2.25 D. should be considered as ineffective cycloplegia, because there is no agreement between the retinoscopic findings and the cycloplegic acceptance. It is in patients with such a residual accommodation that one notices an unstable neutralization point during retinoscopy. Above this, mydriasis with poor cycloplegia exists. In analysis of the inadequate cycloplegic effect in our series of 200 patients (400 eyes) examined with hydroxyamphetamine and homatropine, one observes that 44 patients, or 22 per cent of the total, had 2.50 D. or more of residual accommodation. Of this group, 14 patients were less than 20 years of age; 14 were between the ages of 20 and 30, and 16 were between the ages of 30 and 40. Of these 44 patients, 41 were Negroes. Of the entire group of 200 patients, 81 were Negroes. Thus, approximately 50 per cent of the Negro patients had poor cycloplegia with this combination. The results for an analogous series of 200 patients with the

dibutoline-homatropine cycloplegia were likewise analyzed. Eighteen of these patients had 2.50 D. or more of residual accommodation. Only 3 in this group were more than 20 years of age. The oldest patient was 26 years of age. Of these 18 patients, 17 were Negroes. Of the entire group of 200 patients, 75 were Negroes.

Further analysis of the results with these two combinations of drugs in a series of 100 eyes shows that in 28 eyes residual accommodation was the same with the two combinations, that in 54 eyes it was less with homatropine and dibutoline and that in 18 eyes it was less with homatropine and hydroxyamphetamine.

Ever since these examinations of the synergistic effect of the drug were made, I have used this combination with over 200 patients in private practice. The residual accommodation was more than 2.50 D. in only 3 patients (6 eyes). These 3 patients were of the Negro race. Many of these 200 patients had previously been examined by the 2 drop method with homatropine and hydroxyamphetamine, and it was interesting to observe the great number who accepted more plus sphere with the dibutoline combination than in their previous examinations.

Since Nov. 1, 1948, we have used a solution of 2.5 per cent of dibutoline sulfate and 2 per cent homatropine hydrobromide (equal parts) routinely in the clinic of the Wills Hospital and have charted the amount of residual accommodation. We have observed a total of almost 1,000 eyes, of which only 6 per cent had inadequate cycloplegia, and in all but 1 instance the poor cycloplegic effect was observed in darkly pigmented Negroes. The ophthalmologic clinic at the Philadelphia General Hospital was likewise supplied with this combination. Fifty patients (100 eyes) were examined. Cycloplegia was adequate in all but 8 per cent. Again, significantly, poor effect was noted in darkly pigmented Negroes.

RECOVERY FROM 2 PER CENT HOMATROPINE HYDROBROMIDE AND 2.5 PER CENT DIBUTOLINE SULFATE

In order to determine the duration of cycloplegia, a group of 50 private patients were examined and their eyes refracted, and their residual accommodation was measured. After six to eight hours, on their return, cycloplegic correction was placed before their eyes and their residual accommodation again measured. This procedure was repeated in twenty-four hours, again in thirty-two hours on patients in whom the cycloplegic effect had not worn off, and again in forty-eight hours if the effects had still not disappeared (table 3). No instance of sensitivity to dibutoline has been observed in any of the patients on whom the drug was used, either in the clinics or in private practice.

EFFECTIVENESS OF VARIOUS CYCLOPLEGICS

Since atropine is generally conceded to be the most effective cycloplegic, we decided to measure the residual accommodation produced by this drug. We studied a group of 50 patients between the ages of 12 and 16 years. The results for 97 eyes were analyzed (3 were amblyopic). All these patients had 1 per cent atropine sulfate solution instilled in each eye three times daily for three days preceding their examination. Of the 97 eyes, 95 had between 0.50 and 1.75 D. of residual accommodation. The remaining 2 had 2.00 D. of accommodation.

On the basis of the effect of atropine, one may conclude that the ideal cycloplegic should leave a residual accommodation of not more than

TABLE 3.—*Time Required for Recovery from Homatropine and Dibutoline*
(50 Patients)

Duration, Hours	Number of Eyes
8	2
24	20
32	36
48	42

TABLE 4.—*Effectiveness of Various Cycloplegics in Producing 2.00 D. or Less of Residual in All Patients Regardless of Race*

Accommodation	
1% atropine sulfate	100%
3.8% dibutoline sulfate and 2% homatropine hydrobromide	68%
5% dibutoline sulfate	63%
6% homatropine hydrobromide and 1% hydroxyamphetamine hydrobromide ophthalmic	61%
1% homatropine hydrobromide	61%

2.00 D. When the previous figures are reanalyzed on this basis, the cycloplegic effectiveness of the various drugs may be charted (table 4).

CONCLUSION

In a study to determine the comparative effectivity of dibutoline sulfate as a cycloplegic, the following observations were made:

1. When used alone, dibutoline sulfate possesses no advantage over homatropine hydrobromide or a combination of homatropine hydrobromide and hydroxyamphetamine (paredrine®) hydrobromide ophthalmic.

2. When dibutoline is used synergistically with homatropine, the amount of residual accommodation is less than that of either drug alone.

3. Recovery of accommodation after the use of dibutoline and homatropine is complete within forty-eight hours.

4. Inadequate cycloplegia from drugs other than atropine occurs predominantly in the Negro race regardless of the cycloplegic used.

(*a*) Forty-one of 81 Negroes had inadequate cycloplegia with homatropine and hydroxyamphetamine.

(*b*) Seventeen of 75 Negroes had inadequate cycloplegia with homatropine and dibutoline.

5. No local or systemic toxic effects due to dibutoline, either alone or in combination, were noted.

6. Atropine sulfate when used for three days prior to examination is still the most effective cycloplegic available.

ACUTE RETROBULBAR NEURITIS

Report of Two Cases

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HONOLULU, T. H.

THE ACUTE form of retrobulbar neuritis is characterized by (1) rapid loss of vision; (2) the presence of a central or paracentral scotoma; (3) a normal fundus, in 85 per cent of cases, and swelling of the disk in 15 per cent (Werner [1]); (4) pain on movement of the eyes and on pressure on the globe, and (5) occasional peripheral field defects. This syndrome has been extensively described by Duane [2] and Duke-Elder,[3] and more recently by Duggan [4] and others. However, most of the reports have been of cases of partial loss of vision, whereas cases of acute bilateral retrobulbar neuritis with total blindness and subsequent restoration of normal vision have not been adequately recorded.

Fuchs [5] reported in detail 2 cases of bilateral involvement with complete loss of vision without recovery and referred to the condition as "malignant retrobulbar neuritis." Lo Wen-Bin [6] reported a case in China with unilateral blindness and recovery of vision to 6/12. Werner [1] described 2 cases of severe retrobulbar neuritis with bilateral swelling of the disk; both patients received adequate treatment but remained almost totally blind. A report of 2 cases with total blindness and subsequent recovery of vision is submitted.

REPORT OF CASES

CASE 1.—N. A., a man aged 31 of Japanese descent, was admitted to Queen's Hospital on Dec. 18, 1946, with the history of onset of mild rhinitis a week prior

1. Werner, L. E.: Retrobulbar Optic Neuritis, Tr. Ophth. Soc. U. Kingdom **45**:376, 1945.

2. Duane, A.: Fuchs's Textbook of Ophthalmology, Philadelphia, J. B. Lippincott Company, 1923.

3. Duke-Elder, W. S.: Text Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3.

4. Duggan, W. F.: Acute Retrobulbar Neuritis as a Manifestation of Acute Localized Tissue Anoxia, Arch. Ophth. **25**:299 (Feb.) 1941.

5. Fuchs, A.: Malignant Retrobulbar Neuritis, Arch. Ophth. **41**:60 (Jan.) 1949.

6. Lo Wen-Bin: Retrobulbar Neuritis, Am. J. Ophth. **31**:1309 (Oct.) 1948.

to his admission, followed two days later by total blindness of the left eye. Progressive and gradual reduction of vision of the right eye then developed.

Three years previously he had experienced slight numbness of the left side of the face and a tingling sensation of the left arm; he was hospitalized for observation but recovered and was discharged before a diagnosis was established. His general health had been good, and until the onset of his present illness he had engaged daily in the strenuous sport of deep sea diving. He drank alcohol only occasionally and smoked a few cigarets daily. There was no evidence of exposure to any toxic agents.

Ophthalmologic Examination.—Vision was 6/90 in the right eye. There was total loss of perception for red and green, but some perception for blue was present. The pupil reacted sluggishly to stimulation with light. There was no light perception in the left eye, and the pupil was dilated to 5 mm. and fixed. The extraocular muscles were normal. The ciliary vessels were slightly injected, and the eyeballs were tender to touch. Tension was normal. The optic disks were slightly hyperemic, but the fundi were otherwise normal. Perimetric examination of the right eye, with a 2 degree white test object, showed a round absolute central scotoma of 10 degrees. There were no peripheral scotomas.

Other Examinations.—The patient was in good general physical condition. Rhinologic examination, which included an irrigation of the sinuses and roentgenologic examination, was noncontributory. Neurologic examination revealed no abnormality. Serologic tests, a complete blood count, urinalysis and determination of the sedimentation rate gave normal results. The spinal fluid pressure and cell count were normal. A roentgenogram of the pituitary fossa showed normal size and contour. The pineal gland contained numerous small calcific deposits.

Treatment.—Treatment consisted of administration of erythrityl tetranitrite U. S. P., 0.03 Gm. every four hours; nicotinic acid, 0.05 Gm. every six hours, and penicillin, 300,000 units daily. Typhoid and paratyphoid vaccine U. S. P. (60,000,000 to 300,000,000 organisms) was given every other day for four doses. Penicillin was discontinued after ten days, and erythrityl tetranitrite and nicotinic acid were discontinued after twenty-two days.

Progress.—On the second hospital day vision was totally abolished in both eyes. The left optic disk was elevated 2 D., and a flame-shaped hemorrhage was present on the temporal edge of the disk. There was no change until the thirteenth hospital day, when the patient began to perceive light in the temporal quadrant of the right eye and the pupil began to react to stimulation with light. Ten days later (January 11) he was able to count fingers at 1 meter, but there was still no light perception in the left eye. The swelling of the disk had receded, but both nerve heads showed pallor of the temporal halves. On February 12, when he was discharged from the hospital, light perception had appeared in the left eye. Vision of the right eye was equal to counting fingers at 4 meters. There was gradual and progressive improvement of vision, and six weeks later (March 29) vision was 6/6 in the right eye and 6/400, with an absolute central scotoma of 4 degrees, in the left visual field. The patient was able to recognize blue and green, but red was seen with difficulty. On June 23, 1949 vision was 6/6 in the right eye and 6/30 in the left eye. There were moderate pallor of the temporal halves of the disks, infiltration of connective tissue in the physiologic cups and attenuation of retinal arterioles. There was no scotoma of the right visual field, but an absolute round central scotoma of 3 degrees remained in the left visual field.

CASE 2.—M. C., aged 30, a housewife of Chinese descent, was admitted to Queen's Hospital on Dec. 22, 1946, with a history of onset of severe frontal headaches six days prior to admission, followed the next day by failing of vision in the left eye. On the second day of her illness, when the left eye became blind, vision in the right eye also began to fail. There was no history of any serious illness or infection or of exposure to a toxic substance.

Ocular Examination.—Vision was limited to perception of hand movements in the right eye and to light perception in the left eye. The pupils were round and dilated to 5 mm. They reacted sluggishly to light. The extraocular movements were normal. The right fundus revealed slight hyperemia of the nerve head and attenuation of the retinal arterioles. There was no edema of the retina. The left fundus was similar to the right. The following morning there was no light perception in either eye. The pupils were dilated and fixed.

Other Examinations.—The general physical condition of the patient was good. Neurologic examination revealed nothing abnormal. Rhinologic and roentgenologic examinations showed no evidence of disease of the paranasal sinuses. In roentgenograms the pituitary fossa and the optic foramens appeared to be of normal size. The Wassermann reaction of the blood was negative. Complete blood count, urinalysis and determination of blood sugar gave normal results. The spinal fluid was under normal pressure, and the cell count and colloidal gold curve were normal.

Treatment.—Treatment consisted of use of pentobarbital sodium for sedation and administration of erythrityl tetranitrite, 0.03 Gm. every four hours, and penicillin, 300,000 units daily. Typhoid and paratyphoid vaccine (30,000,000 organisms) was given on the second day, but this treatment was not continued because of severe headaches.

Progress.—On Dec. 26, 1946, the patient noted light perception in the left eye. No hemorrhages were seen, and the maximum elevation of the disk was 1 D. On Jan. 3, 1947, when she was discharged from the hospital, vision was 6/60 in the right eye and was limited to counting of fingers at 1 meter in the left eye. There was a return of perception for blue. A week later she could distinguish green and blue but was not able to recognize red. Pallor of the temporal halves of the disks was noted. The pupils had returned to normal size. On March 30 vision was 6/30 in the right eye and 6/90 in the left eye; on Aug. 6, 1947, 6/12 in the right eye and 6/60 in the left eye; in January 1948, 6/7.5 in the right eye and 6/30 in the left eye, and in June 1949, 6/6 in the right eye and 6/15 in the left eye. There was no scotoma in the right eye, but a round central relative scotoma of 2 degrees was present in the left eye.

COMMENT

The etiologic factors in these 2 cases are undetermined, although the patients were studied carefully by various members of the hospital staff. Most writers[7] are agreed that multiple sclerosis accounts for the greatest number of cases of retrobulbar neuritis. The neurologic consultants who examined the patients found no evidence of multiple sclerosis, and their opinions are supported by the fact that there are no known

7. Benedict, W. L.: Retrobulbar Neuritis and Diseases of Nasal Accessory Sinuses, Arch. Ophth. 9:893 (June) 1933. Duke-Elder.[9]

cases of multiple sclerosis among the natives of the Territory of Hawaii. Duke-Elder stated, "It seems probable that many cases in which the etiology is unknown and in which no further general symptoms develop, are the expression of an unknown virus with neurotrophic tendencies." It is likely that the etiologic agents in the 2 cases described fall within this category.

Duggan,[4] Moon [8] and others have interpreted the pathologic picture as the result of arterial spasm with dilatation and increased permeability of the capillaries, leading to localized edema and tissue anoxia. In the treatment of this condition, a misleading factor in determining the effectiveness of any drug is the tendency to spontaneous recovery in the majority of cases. On the basis of the pathologic change, however, treatment should be immediate and directed toward the relief of vasospasm of the peripheral arterioles. As advocated by Duggan, Ravin [9] and others, any of the nitrites may be used. Typhoid vaccine, histamine acetylcholine, thiamine hydrochloride and nicotinic acid also act as vasodilators. They may be used as adjuvants to the nitrites. The evidence that the nitrates administered in the present cases led to recovery was only presumptive. It is doubtful whether penicillin was of any value. These 2 cases are reported to show the possibilities of recovery of vision even in the worst cases of acute retrobulbar neuritis.

1147 Union Street.

8. Moon, V.: Shock and Related Phenomena, New York, Oxford University Press, 1938.

9. Ravin, L. C.: Vasodilators for Acute Optic Neuritis, Am. J. Ophth. **26**: 188 (Feb.) 1943.

HYPERPHORIA

A Statistical Study

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TOTAL hyperphoria is made up of two parts: (*a*) manifest hyperphoria, which appears almost immediately after the two eyes are dissociated, and (*b*) latent hyperphoria, which appears only after prolonged dissociation of the two eyes. Various tests for heterophoria elicit varying amounts of hyperphoria because they convert varying amounts of latent hyperphoria into manifest hyperphoria, which may be observed and measured.

PURPOSE OF THE STUDY

This study is essentially statistical in character. A statistical study of hyperphoria will elicit some general facts about the condition. There are, unfortunately, too few such studies on record.

THE SAMPLE

The sample was composed of 1,476 private patients. It was a selected sample in that all were persons presenting themselves at an ophthalmologist's office. Some came because of asthenopia, but many came for other reasons, such as a foreign body in the eye or conjunctivitis. All patients had refraction, and glasses were prescribed when indicated. It is believed that the sample represents a reasonably fair cross section of the daily practice of the average ophthalmologist.

METHODS OF TESTING

Measurements were made for hyperphoria on all patients with a Maddox rod. Some patients had a second determination with the screen and parallax test; still others had a Maddox wing test. Only the results from the Maddox rod test are considered in this report.

The Maddox rod used was mounted on, and a part of, a Stevens phorometer. A white Maddox rod could be easily rotated into position before either eye. Two rotary prisms were available on the instrument. One had a total strength of 2 D. and was calibrated in units of 0.2 D. It was capable of being read accurately to

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This study was made under a contract with the Office of Naval Research as Project N6onr-202, Task Order I, NR 141-022.

the nearest 0.1 D. The second rotary prism had a total strength of 30 D., was calibrated in units of 1.0 D. and could be read accurately only to the nearest 1.0 D.

The muscle light in the test for far vision was 1.0 cm. in diameter and was located 20 feet (6 meters) from the patient. The muscle light in the test for near vision was a May ophthalmoscope with the head removed. In determinations of hyperphoria at near in the reading position, the head of the phorometer was tilted downward, so that measurements were made with the eyes actually in the reading position. The light was held at a distance of 13 inches (33 cm.) from the patient in this test.

All patients were routinely tested with the Maddox rod and rotary prism before the right eye. If less than 0.5 △ of hyperphoria was found at both near and far, no other measurement was made of vertical phoria. If 0.5 △ or more of hyperphoria was found at either near or far, the Maddox rod was shifted to the left eye, and the measurements for near and far were repeated. The rotary prism was shifted with the Maddox rod.

If the hyperphoria was greater than 2.0 △, the 30 D. rotary prism was used, and additional measurements were made with the screen and parallax test, and usually with the Maddox wing test as well.

The eye behind the Maddox rod was considered the nonfixing eye, the patient's attention being constantly directed toward the muscle light. Data were recorded with first the left and then the right eye fixing at distances of both 20 feet and 13 inches.

CRITERIA OF CLINICAL SIGNIFICANCE

Clinical significance was judged almost solely on the basis of the presence or absence of symptoms associated with the hyperphoria.

In the absence of symptoms, the hyperphoria was not considered clinically significant, with a single exception, to be mentioned shortly.

If hyperphoria was present and the patient complained of asthenopia, a careful refraction was performed, glasses were prescribed and the patient was requested to wear the glasses constantly during waking hours for a period of one month. If at the end of the month the patient was free from symptoms, hyperphoria was not considered clinically significant.

If symptoms persisted at the end of one month prisms were then given—usually as a clip-on lens—and a trial period from two to three weeks was prescribed. If symptoms had disappeared at the end of this trial period, the hyperphoria was considered clinically significant, and prisms were prescribed for permanent wear, having been incorporated into the patient's lenses.

An occasional patient with a comparatively large amount of hyperphoria associated with obvious symptoms, chiefly panoramic in character, was given prisms immediately, almost invariably with complete relief.

If a patient's hyperphoria was relatively great and there were few, if any, symptoms but there was definite evidence of suppression and poor fusion, prisms were prescribed. If the suppression disappeared, the hyperphoria was considered clinically significant.

RESULTS

Incidence.—How frequent is hyperphoria? A series of 1,476 consecutive patients were carefully studied. In 521 hyperphoria of 0.5 Δ or more was found with the Maddox rod test. This is an incidence of 35 per cent of the sample studied. About 1 of every 3 patients had 0.5 Δ or more of hyperphoria. Certainly, 1 of every 3 patients does not have symptoms associated with hyperphoria. In what percentage of patients is the hyperphoria clinically significant? Using the criteria of significance already outlined, 90 of the 521 patients (17 per cent) had clinically significant hyperphoria. Ninety patients represent 6 per

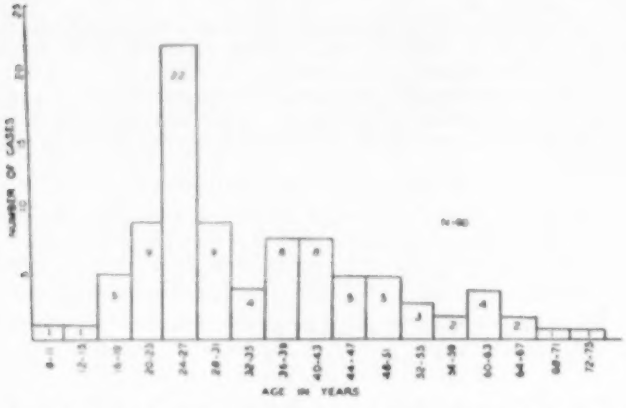

Chart 1.—Age distribution histogram for 90 patients with clinically significant hyperphoria.

cent of the entire sample of 1,476 patients. Thus, while 1 of 3 patients may be expected to have 0.5 Δ or more of hyperphoria, only about 1 of 20 patients will have hyperphoria that is clinically significant. Of the 521 patients, 90 had significant and 431 nonsignificant hyperphoria. In our experience, less than 0.5 Δ of hyperphoria at both near and far, as measured by the Maddox rod, was never clinically significant; larger amounts might or might not be significant.

Relation to Age.—Histograms for age distribution are shown for both clinically significant (chart 1) and nonsignificant (chart 2) hyperphoria. The ranges for the two groups are almost identical. The peak in both groups lies at about 26 and 27 years of age.

Hansell [1] stated that 33 per cent of all cases of hyperphoria occurred in patients under 30 and that the remaining 67 per cent was found in persons past the age of 30. They offered the tentative explanation that in youth a strong fusion faculty and a superabundance of elasticity render perfect coordination easy. With maturity in later years, latent tendencies become manifest. The implication that hyperphoria increases with age is quite clear. The findings in the present study are not in agreement. Fifty-three per cent of patients with hyperphoria of 0.5 Δ or more are under 30 years of age. This is about what would be expected on the basis of the present average life expectancy. A previous study [2] has shown no significant relation of the lateral phorias to age. It would appear that the same is true in the case of hyperphoria.

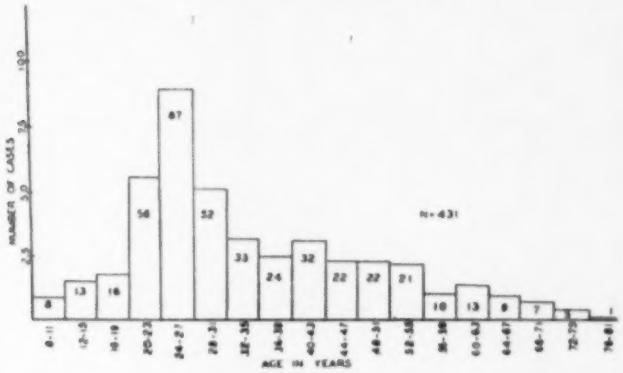

Chart 2.—Age distribution histogram for 431 patients with clinically non-significant hyperphoria.

Visual Acuity.—Stevens [3] described mild amblyopia in one eye as a symptom associated with hyperphoria. He reported on a series of 200 cases in which the average visual acuity in the better eye was 20/30 while that in the poorer eye was 20/50. He concluded that defective visual acuity was the rule rather than the exception in moderate degrees of hyperphoria. His study made no mention of refractive error.

In our series of 521 patients, all had refraction; 441 (84.6 per cent) had equal vision in the two eyes. Of the 90 patients whose hyperphoria

1. Hansell, H. F.: The Ocular Muscles, Philadelphia, P. Blakiston's Son & Co., Philadelphia, 1912.

2. Scobee, R. G., and Green, E. L.: Am. J. Ophth. **31**:427, 1948.

3. Stevens, A. A.: Motor Apparatus of the Eyes, Philadelphia, F. A. Davis Company, 1906.

was judged clinically significant, 66 (73 per cent) had equal visual acuity in each eye after refraction.

Relation of Lateral and Vertical Phoria.—The values for lateral and significant vertical phoria for each patient at 20 feet (chart 3) and at 13 inches (chart 4) are plotted on scatter diagrams. This random scattering is sufficient, without actual calculation of correlation coefficients, to indicate that there is no significant relation between lateral phoria and clinically significant hyperphoria. It should perhaps be stated that the measurements of hyperphoria in clinically significant

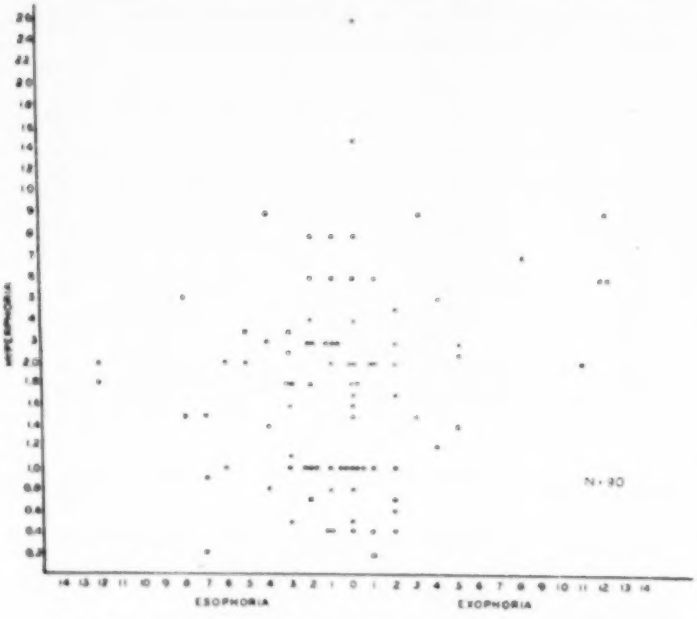

Chart 3.—Scatter diagram showing absence of significant relation between lateral phoria tested at 13 inches (33 cm.) and clinically significant hyperphoria.

cases were recorded for charting only after the patients had been recorded emmetropic with glasses for one month.

Similar scatter diagrams for the cases of nonsignificant hyperphoria showed essentially the same thing at both 20 feet and 13 inches and are not reproduced.

Prisms and Hyperphoria.—Many oculists are of the opinion that the prescription of vertical prisms in cases of hyperphoria will almost invariably cause the manifest hyperphoria to increase. In order to

investigate this possibility, the 90 patients with clinically significant hyperphoria were carefully followed. The follow-up period was not longer than five years or shorter than one year for any one patient. The results are interesting.

Sixteen of the 90 patients (18 per cent) showed an increase in their manifest hyperphoria after constantly wearing vertical prisms. The remaining 82 per cent showed no increase at all, a fact which should make many physicians less hesitant to prescribe vertical prisms for the relief of symptoms associated with hyperphoria.

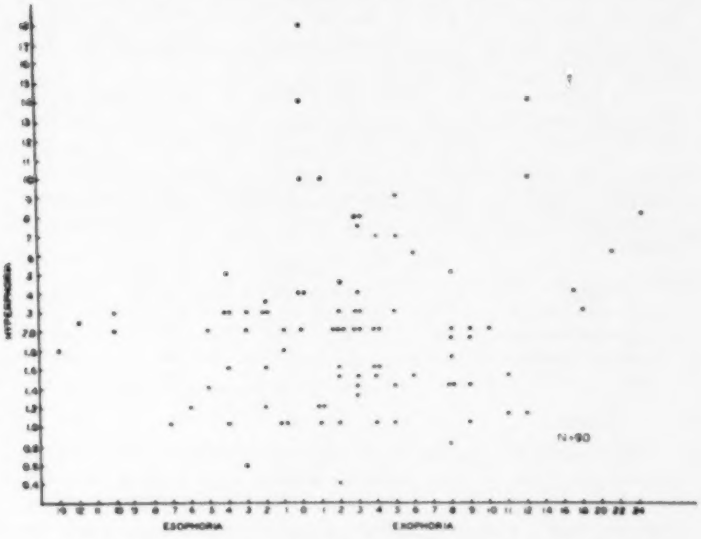

Chart 4.—Scatter diagram showing absence of significant relation between lateral phoria tested at 20 feet (6 meters) and clinically significant hyperphoria.

The Involved Muscle.—The cause of hyperphoria has long been, and for that matter still is, in dispute. White [4] stated the belief that in 98 per cent of all cases of hyperphoria the origin was paretic. We must include ourselves among those who disagree, but it is not intended to discuss the etiology of hyperphoria in this paper.

There can be little argument that hyperphoria that is nonparetic in origin is, broadly speaking, innervational. Muscles may appear either to overact or to underact because of excessive or insufficient innervation,

4. White, J. W.: Hyperphoria: Diagnosis and Treatment, Arch. Ophth. 7:739 (May) 1932.

respectively. It will be noted that we have headed this section "The Involved Muscle" rather than "The Paretic Muscle." The reason should be clear.

White pointed out several steps in the identification of the involved muscle; he did this in rather a haphazard fashion, spreading the points over several papers. His steps have been arranged into a definite scheme,[5] and the details are readily available to those interested in pursuing the matter further. Suffice it to say that the scheme is based on the fact that the vertical rectus muscles are the most efficient vertical movers when the eyes are in the primary position. In the reading position, however, the oblique muscles are more efficient as vertical movers than are the vertical rectus muscles. Several authors have pointed out why this should be so.[6]

The scheme just mentioned was utilized in identification of the "involved" muscle in the cases in this series in which it was applicable. The results are of interest from the standpoint of frequency of involvement of the various vertically acting muscles—a question still in some dispute. With respect to the figures in the tabulation, we wish to make it clear that they refer only to an "involved" muscle, not to a "paretic" muscle.

Muscle	Significant Hyperphoria	Nonsignificant Hyperphoria	Totals
Inferior oblique	32	123	155
Superior oblique	29	117	146
Superior rectus	15	90	105
Inferior rectus	14	59	73
Totals	90	389	479

The frequency of seeming involvement of the inferior oblique muscle deserves comment. It is of particular interest to us because we are of the opinion that picked or isolated paralysis of that muscle alone is extremely rare. Isolated paralysis of the inferior oblique should be accompanied with an increase in size of the pupil and some loss of accommodation on the side of the paretic muscle. Neither finding was present in any of the cases of hyperphoria in this series, even though in a large number the inferior oblique was apparently involved. At present we are forced to interpret this as evidence that in many cases hyperphoria is innervational in origin, rather than paretic. This is, of course, in disagreement with White.[1] We feel that the present state of our knowledge on the subject does not allow further comment, and we merely report the figures as being thought provoking and as material for further study and discussion.

5. Scobee, R. G.: The Oculorotary Muscles, St. Louis, C. V. Mosby Company, 1947.

6. White,[1] Scobee,[5] Adler, F. H.: Am. Ophth. Soc. **43**:255, 1945.

SUMMARY AND CONCLUSIONS

A series of 1,476 consecutive patients were examined for hyperphoria by the Maddox rod test; 521 patients had 0.5 Δ or more of hyperphoria. Clinical significance of the hyperphoria was judged primarily on the basis of associated symptoms. From the results in the present series, 1 of every 3 patients may be expected to have 0.5 Δ or more of hyperphoria, but only 1 of 20 patients will have hyperphoria that is clinically significant.

There was no significant relation between age and hyperphoria. Age distribution curves are shown both for nonsignificant and for significant hyperphoria.

Visual acuity was equal in the two eyes of 85 per cent of patients with hyperphoria, a finding in disagreement with a previously reported study of Stevens.

There was no relation between lateral and significant vertical phorias at either 20 feet (6 meters) or at 13 inches (33 cm.).

Eighteen per cent of patients with clinically significant hyperphoria showed an increase in manifest hyperphoria after prescription of vertical prisms for constant wear; in the remaining 82 per cent the hyperphoria remained constant in amount when the prisms were worn.

The order of frequency of the involved muscles was found to be as follows: (1) inferior oblique, (2) superior oblique, (3) superior rectus and (4) inferior rectus. It is to be emphasized that this is a frequency of the "involved" muscle, and not of the "paretic" muscle.

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AGE NORMS OF REFRACTION AND VISION

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EDWARD JACKSON,[1] in his "Norms of Refraction," stated: Norm is defined as: "A rule or authoritative standard: a model, a typical example." In the same article, Dr. Jackson stated:

> Norms of refraction are so important that they have been assumed or accepted on the observance of a few eyes. But they will be exact and useful only when the averages and changes have been noted for a great many. The records of a large city clinic, or the facilities of a university laboratory are worth very little in seeking such norms. They must represent the result of a large number of clinical observations made with care by established methods, over long periods. The return of clinic patients is so uncertain and irregular that very little can be learned from them in such an investigation.

Jackson also suggested:

> The average spherical refraction be considered as an average of the refraction of the principal meridians of regular astigmatism.

Optically, the average of the two meridians of regular astigmatism is the spherical equivalent.

I use the words "spherical equivalent" to describe this refraction. It was obtained by using one-half the cylinder added to the sphere algebraically, as suggested by J. C. Copeland.

The only eyes, except for those of the special old age group, included in this study of refraction and visual averages were healthy eyes with clear lenses.

By vision is meant the visual acuity measured at 5 meters on a 1 minute angle on the metric chart, each letter subtending a 5 minute angle over-all. For children and illiterates a similar metric E chart was used. Different charts were used in testing the two eyes. A standard illumination of 10 foot candles was used.

Vision was taken after refraction with cycloplegia, with correcting lenses as indicated. All the compilations were based on the results of

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Read before the Section on Ophthalmology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

1. Jackson, E.: Norms of Refraction, Tr. Sect. Ophth., A. M. A., 1931, p. 174; ibid. J. A. M. A. **96**:132 (Jan. 9) 1932.

cycloplegic refractions done by myself in private practice. Except in the case of young children, 2 per cent homatropine hydrobromide was administered as follows: If the patient's accommodation was 2 D. or less, 1 drop was placed in each eye every fifteen minutes until four instillations were made (one hour). If the accommodation was over 2 D., 1 drop was instilled in each eye every fifteen minutes for each ½ D. of accommodation up to and including 4 D. (e. g., 6 drops for 3 D. of accommodation). Not more than 8 drops in each eye were used in any patient unless the refraction indicated that cycloplegia was not complete; then more drops were instilled.

For young children, 1 per cent atropine sulfate ointment was used at least three times a day for two days preceding the morning of the refraction. Just before the retinoscopic examination, 1 drop of 1 per cent aqueous solution of atropine sulfate was instilled in each eye and pressure exerted for a few minutes on each lacrimal punctum.

Only patients who had vision of 5/7.5 or better, except those under 8 years of age or in the old age group, were used in determining the changes in spherical equivalent refraction and vision. All diseased eyes (including those with amblyopia ex anopsia) were excluded in the study of refraction and vision. Also excluded were all patients with myopia over — 6.00 D. and all with hypermetropia over + 8.00 D.

PROCEDURES

Rules for Calculation of Annual Age Variations.—To calculate the annual variations of two refractions, the following rules are observed:

1. All refractions are reduced to their spherical equivalents. The spherical equivalent of a compound refraction is equal to the total sphere added algebraically to one-half the cylinder, and the spherical equivalent of a simple cylinder is equal to one-half the cylinder of the same sign.

2. To obtain the difference of two spherical equivalent refractions of like signs, the lesser is subtracted from the greater. If the signs are different, the refractions are added algebraically and the sign of the greater used. If the cylinder has increased, the plus sign is used; if it has decreased, the minus sign is used e. g.,

— 1.25 cyl. (old)
— 0.75 cyl. (new)
— 0.50, or difference in cylinder of — 0.50.

3. The change in spherical equivalent of any two refractions is divided by the number of years elapsed between examinations to obtain the yearly variable.

Ophthalmologists have used two methods in obtaining the annual age variation of a refraction: the single and the multiple method.

The Single Method.—In the single method only one examination is made of each patient for most of the observations.

1. A large number of refractions are taken for any one age year of life. Each refraction is reduced to its spherical equivalent.

2. The arithmetical average for that age is obtained.

3. The same procedure is carried out for the age year above and below. The difference of these averages will be the annual age variation of the spherical equivalent for that year.

4. All the cylinders are added, regardless of signs, to obtain the average cylinder for one age year.

5. The same thing is done for the year above and below.

6. The difference of these averages gives the annual age variation of the cylinder for that year.

The Multiple Method.—In the multiple method, several refractions are made on the same subject at different years of age. The change in spherical equivalent between any two refractions is divided by the number of years between these refractions. Data in an illustrative case follow:

Age	Spherical Equivalent (S. E.)
15	—2.00 D.
7	0.00
Change in S. E. in 8 year interval	—2.00 D.
Annual age variation	—0.25 D.
18	—2.50 D.
15	—2.00
Change in S. E. in 3 year interval	—0.50 D.
Annual age variation	—0.166 D.

Most statistically minded ophthalmologists, such as E. V. L. Brown,[2] prefer the multiple method. Brown stated:

> Yet such studies are in the nature of things inaccurate in comparison with data obtained on the same person, studied year after year.

In making these calculations, I found that for groups of a few hundred subjects the multiple method was nearly fourteen times as accurate as the single method, as determined by the probable error and the mean deviation.

2. Brown, E. V. L.: Net Average Yearly Change in Refraction of Atropinized Eyes from Birth to Beyond Middle Life, Arch. Ophth. **19**:722 (May) 1938.

I used a total of 14,868 ocular refractions in the single method and 20,702 ocular refractions in the multiple method, or a total of 35,570 ocular refractions. The average interval between cycloplegic refractions was 5.03 years.

In this study, "eyes examined" means that cycloplegic refractions were made or visual acuities taken at intervals of one or more years. The same eye was often examined many times during the patient's life.

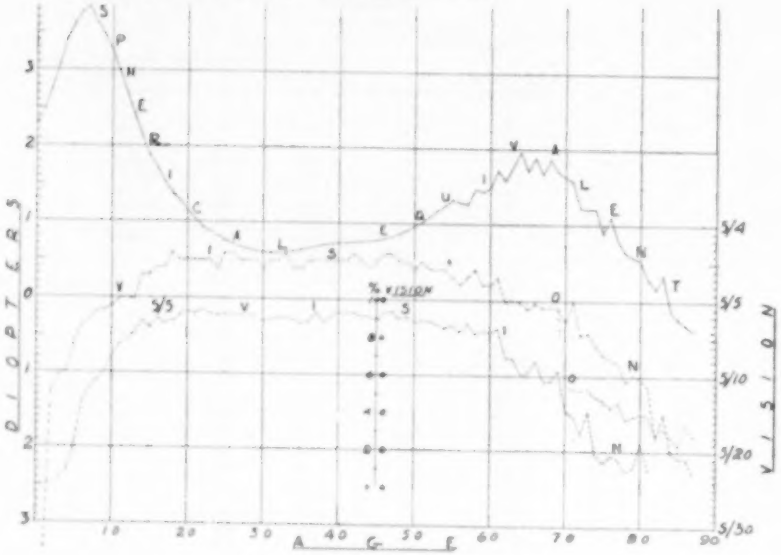
TABLE I.—*Comparison of Annual Age Variations in the Brown and the Present Series*

		Brown Series		Slataper Series		
Age	No.	Annual Age Variation, D.	Difference, D.	Annual Age Variation, D.	No.	Average Annual Age Variation, D.
2	79	+0.41	0.132	+0.256	34	+0.334
3	167	+0.43	0.096	+0.337	42	+0.383
4	231	+0.27	0.040	+0.310	90	+0.290
5	457	+0.23	0.004	+0.226	114	+0.228
6	549	+0.17	0.012	+0.158	118	+0.164
7	397	+0.02	0.045	+0.065	108	+0.042
8	469	−0.11	0.007	−0.207	140	−0.159
9	533	−0.19	0.044	−0.146	224	−0.168
10	488	−0.27	0.030	−0.240	172	−0.255
11	466	−0.27	0.000	−0.307	224	.....
12	469	−0.27	0.029	−0.299	480	.....
13	456	−0.29	0.016	−0.306	484	.....
14	402	−0.23	0.062	−0.292	497	.....
15	374	−0.17	0.086	−0.256	504	.....
16	342	−0.17	0.000	−0.167	510	.....
17	295	−0.15	0.044	−0.194	480	.....
18	261	−0.10	0.049	−0.149	456	.....
19	206	−0.10	0.035	−0.135	406	.....
20	158	−0.08	0.056	−0.136	466	.....
21	140	−0.05	0.067	−0.117	510	.....
22	105	−0.05	0.026	−0.086	564	.....
23	150	−0.06	0.020	−0.080	520	.....
24	160	−0.05	0.013	−0.063	526	.....
25	157	−0.04	0.012	−0.052	582	.....
26	125	−0.03	0.005	−0.035	592	.....
27	139	−0.02	0.016	−0.036	570	.....
28	116	−0.04	0.008	−0.032	606	.....
29	117	−0.005	0.020	−0.025	634	.....
30	110	−0.001	0.015	−0.016	648	.....
	8,914		1.104		11,328	
	Total difference.....			1.104		
	Average difference.....			29 ±0.038		

In the oldest group, that of the last twenty-one years, in which the annual average was 57 eyes per year, one-half the probable error was corrected by plotting each year on a diagonal line from 68 to 87. This reading was averaged with the original figures for each year. This doubled the number of ocular compilations and made for accuracy. This principle is often used in civil engineering.

Brown used compilations of 8,104 eyes of patients of ages from 1 to 30 inclusive, as shown in table 1. Since he had many more patients from 1 to 6 years of age than I, I include his statistics for ages from 1 to 10 years, which give a better over-all picture of the age variations for these years.

It will be noted that his annual age variations are very close to mine, the difference being ± 0.038 D. Hence, in table 1 I have given the averages of our two figures for each of the first ten years of life. My table 2 and graph (chart) include the cases from Brown's statistics for the group from 1 to 10 years of age (table 2).



Age norms of refraction and vision.

For the years (below 11) for which my statistics were weak, Brown [2] had many more cases. For the group below 11 years of age, he had a total of 3,138 eyes and I had 1,062 eyes, the total being 4,200 eyes.

Age Norms for Spherical Equivalent Refraction.—The four types of age variations from the average of + 2.32 D. at birth are tabulated:

Hypermetropia of early childhood	Birth to 7 yr.	+ 1.617 D.
Axial myopia of the young	8 to 30 yr.	− 3.327 D.
Hypermetropia of middle age	31 to 64 yr.	+ 1.362 D.
Senile myopia	65 to 87 yr.	− 2.367 D.
These values are shown in the graph		± 8.673 D.

TABLE 2.—*Age Norms of Refraction and Vision*

Age	Spherical Equivalent, D.	Annual Age Variation, D.	Number of Eyes	Vision	Number	Percentage with 20/20 Vision
0	+2.320	.....	...	.....	...	..
1	+2.490	+0.176	16	5/35 (estimated)	...	..
2	+2.830	+0.334	105	5/12/1	7	..
3	+3.213	+0.383	209	5/10.4	59	2
4	+3.503	+0.290	291	5/9.9	92	5
5	+3.731	+0.228	371	5/8.2	115	22
6	+3.895	+0.164	467	5/6.7	207	44
7	+3.967	+0.042	555	5/6.4	261	52
8	+3.778	−0.159	619	5/6	250	56
9	+3.610	−0.168	757	5/5.8	318	61
10	+3.355	−0.255	638	5/5.6	259	69
11	+3.088	−0.267	224	5/5.1	273	75
12	+2.780	−0.299	480	5/5	305	78
13	+2.483	−0.305	464	5/5.2	321	61
14	+2.191	−0.298	492	5/4.7	255	85
15	+1.935	−0.256	504	5/4.7	243	84
16	+1.768	−0.167	510	5/4.6	258	89
17	+1.574	−0.194	480	5/4.6	201	87
18	+1.425	−0.149	456	5/4.4	270	88
19	+1.290	−0.135	405	5/4.5	283	91
20	+1.152	−0.138	495	5/4.5	319	85
21	+1.035	−0.117	510	5/4.5	367	92
22	+0.949	−0.086	504	5/4.5	287	94
23	+0.869	−0.080	520	5/4.5	337	92
24	+0.806	−0.063	536	5/4.6	413	91
25	+0.754	−0.052	562	5/4.4	419	89
26	+0.719	−0.035	532	5/4.4	361	92
27	+0.685	−0.034	570	5/4.5	370	91
28	+0.651	−0.034	606	5/4.5	410	91
29	+0.626	−0.025	634	5/4.5	400	91
30	+0.610	−0.016	648	5/4.6	386	88
31	+0.603	−0.007	600	5/4.5	306	89
32	+0.605	+0.002	702	5/4.5	394	88
33	+0.617	+0.012	708	5/4.4	339	92
34	+0.639	+0.013	702	5/4.6	332	89
35	+0.647	+0.018	719	5/4.6	367	87
36	+0.662	+0.015	754	5/4.5	289	88
37	+0.687	+0.025	726	5/4.5	282	93
38	+0.707	+0.020	702	5/4.5	354	88
39	+0.721	+0.014	702	5/4.5	287	91
40	+0.730	+0.009	800	5/4.5	308	93
41	+0.744	+0.014	782	5/4.5	354	93
42	+0.750	+0.006	722	5/4.4	411	93
43	+0.756	+0.006	725	5/4.5	428	91
44	+0.762	+0.006	718	5/4.6	379	91
45	+0.778	+0.016	714	5/4.5	387	89
46	+0.799	+0.021	708	5/4.4	311	95
47	+0.828	+0.029	712	5/4.4	295	94
48	+0.864	+0.036	638	5/4.5	299	90
49	+0.909	+0.045	614	5/4.5	238	91
50	+0.962	+0.053	582	5/4.6	276	88
51	+1.022	+0.060	566	5/4.5	181	89
52	+1.093	+0.071	452	5/4.6	192	89
53	+1.168	+0.075	432	5/4.6	167	87
54	+1.237	+0.069	378	5/4.6	168	85
55	+1.306	+0.069	350	5/4.7	129	87
56	+1.286	−0.020	375	5/4.8	112	83
57	+1.253	−0.033	368	5/4.7	87	88
58	+1.468	+0.215	300	5/4.6	129	82
59	+1.439	−0.029	274	5/4.8	94	84
60	+1.478	+0.039	231	5/4.8	84	83
61	+1.722	+0.244	197	5/4.7	89	85
62	+1.593	−0.129	204	5/5.2	97	70
63	+1.708	+0.116	135	5/5	79	69
64	+1.972	+0.264	118	5/5.2	78	61
65	+1.720	−0.252	105	5/5.6	84	62
66	+1.896	+0.176	66	5/5.2	50	68
67	+1.682	−0.213	63	5/5.4	33	58
68	+1.879	+0.196	105	5/5.4	42	57
69	+1.715	−0.164	80	5/5.4	60	62
70	+1.602	−0.093	112	5/6.4	100	42
71	+1.574	−0.028	72	5/5	62	36
72	+1.215	−0.359	152	5/7.3	72	29.5
73	+1.201	−0.014	144	5/7.2	58	41
74	+1.211	+0.010	124	5/8.1	56	18
75	+.899	−0.314	116	5/8.6	100	14
76	+1.165	+0.266	72	5/8.8	36	19
77	+0.789	−0.376	44	5/9.1	27	16
78	+0.639	−0.150	36	5/10.8	18	9.5
79	+0.577	−0.062	40	5/9.9	20	12
80	+0.537	−0.040	24	5/10.4	12	24
81	+0.298	−0.249	16	5/11.5	8	10
82	+0.164	−0.134	8	5/18.3	4	..
83	+0.347	+0.183	20	5/15	10	..
84	−0.135	−0.482	8	5/20.1	4	..
85	−0.239	−0.104	8	5/20.9	4	..
86	−0.311	−0.072	8	5/21	4	..
87	−0.395	−0.084	8	5/23	4	..
			34,570		17,286	

Herrnheiser [3] examined 1,918 eyes of newborn children between the ages of 8 and 14 days under atropine cycloplegia. He found that the average refraction was + 2.32 D.

CHANGES OCCURRING WITH AGE

The total change in spherical equivalent during life was ± 8.673 D. It can be seen that from birth to 7 years of age the eye made a gain of + 1.617 D. of hypermetropia, an average of + 0.231 D. per year—the hypermetropic change of early childhood. After the age of 7 years the eye becomes more myopic (or less hypermetropic), until the age of 30. During this period the refraction shifted toward myopia by — 3.327 D., an average of — 0.151 D. per year. Is this axial myopia in the young due to the physiologic stretching of the eyeball? From the ages of 31 to 64 years, the eye had a gradual gain of + 1.362 D. of presbyopic hypermetropia, the hypermetropia of middle age, an average of + 0.04 D. per year.

Parsons [4] stated:

> The hypermetropia which comes on in old age associated with presbyopia is to be attributed to increased refractive index of the cortex of the lens. Straub and Falkenburg consider that it is a dynamic hypermetropia due to loss of tone in the ciliary muscle.

After the age of 64 the refraction becomes more minus, owing to senile changes in the lens. However, the refractive change is only slightly myopic, though fairly constant, until the age of 71 is reached, when there is a marked myopic change. The rapidity of this change is due to the development of senile cataract. The total change of senile myopia from the ages of 65 to 87 was — 2.367 D., an average of — 0.103 D. per year. The greatest annual variation, + 0.231 D., occurred in early childhood, and the least, + 0.04 D., in middle age, the hypermetropia of middle age (chart).

AVERAGE REFRACTION FOR ADULTS

What is the average refraction for adult life, excluding old age, with homatropine cycloplegia? The graph shows that the changes in spherical equivalent were least between the ages of 22 to 55, inclusive. Hence this would be the fairest age on which to base a conclusion.

I took the spherical equivalent for each of these years and corrected their annual age variation to the age of 34 years. The average of these corrected averages to the age of 34 was + 0.629 D. This series consisted of 10,020 eyes, or an average of 295 eyes per year.

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3. Herrnheiser, J.: Die Refractionsentwicklung des menschlichen Auges, Ztschr. f. Heilk. **13**:348, 1892.

4. Parsons, J. H.: The Pathology of the Eye, New York, G. P. Putnam's Sons, 1906, vol. 3, p. 935.

Bothman [5] showed that atropine cycloplegia uncovered, in both myopia and hypermetropia, an average of 0.605 D. more plus refraction than did homatropine cycloplegia. Bothman's average factor was + 0.605 D; my average, with homatropine cycloplegia, was + 0.629 D., a total of + 1.234 D. Therefore, my atropine refraction should be + 1.234 D. This value is practically the same as Brown and Kronfeld's [6] figure for the average adult refraction, or + 1.25 D. under atropine cycloplegia.

VARIATION IN CYLINDER

In a study of the changes in cylinder between 1 and 72 years of age in 15,120 eyes with the single method and in 20,222 eyes with the multiple method, the average change of cylinder was found to be ± 0.066 D. per year, that is, a change of less than 0.1 D. in the strength of the cylinder. The variation in cylinder from year to year was so radical that it became confusing.

The averages for groups of five years were then taken. These groups averaged 2,524 eyes each, and their average variation was ± 0.066 D.—the same as the annual variation. I frequently found a marked change in the cylinder variation in individual patients after a few years—as much as 1.00 D. My conclusion is that there is nothing constant about the average change in the strength of the cylinder as the result of age. However, the age factor does change the axis of the cylinder, as shown by Kronfeld.[7]

The other detailed statistics on variation in cylinder are so inconstant that they are not of sufficient value to justify their inclusion in this article.

COMPARISON OF ANNUAL AGE VARIATIONS IN MYOPIA AND HYPERMETROPIA

A series of 1,704 myopic eyes was checked against one of 2,003 hypermetropic eyes each year from the ages of 8 to 22 years.

	Spherical Equivalent	
Eyes	Total Change	Annual Average Change
Myopic	— 4.326 D.	— 0.288 D.
Hypermetropic	— 2.128 D.	— 0.142 D.
Both myopic and hyperopic	— 2.774 D.	— 0.185 D.

5. Bothman, L.: Homatropine and Atropine Cycloplegia, Arch. Ophth. **7**:398 (March) 1932.

6. Brown, E. V. L., and Kronfeld, P. C.: The Refraction Curve in the U. S. A., with Special Reference to Changes in the First Two Decades, Extrait de Compte-Rendu du XIII Concilium Ophthalmologicum, Amsterdam, The Haag, 1929.

7. Kronfeld, P. C.: Frequency of Astigmatism, Arch. Ophth. **4**:883 (Dec.) 1930.

Therefore the myopic change in the young was twice as great in the myopic as in the hyperopic subjects.

Subject	Average Cylinder
Myopic	0.62 D.
Hypermetropic	0.83 D.
	0.21 D.

The hypermetropic subjects had 0.21 D. more cylinder than the myopic subjects.

From this we can conclude that a hyperopic eye of a certain degree is more apt to have a higher grade of astigmatism than a myopic eye of the corresponding degree [Kronfeld].

Therefore myopia is not due to uncorrected astigmatism.

Of 1,586 myopic eyes, or 793 pairs of eyes, the most myopic had an average cylinder of 0.58 D., and the least myopic, an average cylinder of 0.47 D., a difference of 0.11 D. cylinder, which is unimportant. As already noted, the hypermetropic subjects had 0.21 D. more cylinder than the myopic subjects.

This slight increase in cylinder would not account for the difference in average spherical equivalent between these eyes.

	Average Spherical Equivalent
Most myopic eye	— 1.453 D.
Least myopic eye	— 1.069 D.
Difference	— 0.384 D.

This difference is three times the difference in cylinder.

Since the hypermetropic subjects had 0.21 D. more cylinder than the myopic subjects, I do not believe that the difference of 0.11 D. cylinder for the most myopic eye is the cause of the increased myopia. Of 210 myopic eyes of equal spherical equivalent, the right eye showed an average cylinder of 0.41 D. and the left eye an average of 0.39 D., a difference of 0.02 D. more cylinder for the right eye. In 1,374 myopic subjects, the spherical equivalent for the right eye averaged — 1.325 D. and that for the left eye, — 1.195 D., proving that the right eye is more often myopic than the left eye by 0.130 D.

MENOPAUSAL CHANGES IN ACCOMMODATION

A study of 950 women and 650 men between the ages of 45 and 50, inclusive, showed that the women lost a total of 0.59 D. accommodation, or 0.1 D. more accommodation each year than the men. At the age of 45 the loss was 0.07 D.; at 46, 0.07 D.; at 47, 0.07 D.; at 48 (middle of the menopause), 0.24 D.; at 49, 0.07 D., and at 50, 0.07 D., a total loss of accommodation of 0.59 D. more in women than in men for this

five year period. The study of Duane's [8] table shows the losses for both men and women as indicated:

Age	Loss of Accommodation, D.
45-46	0.5
46-47	0.4
47-48	0.4
48-49	0.2
49-50	0.2
Total loss	1.700 D.

My greater loss in women than in men is 0.59 D. for this period.

The average age of the menopause is 47½ years. Novak [9] stated: "Fifty per cent of all women cease menstruating between 45 and 50 years of age; a quarter below 45 and a quarter above 50 years." Now, one-half the women lose 0.59 D. more accommodation than men in five years. If only one half of these women show the effect of menopause, then 2×0.59 D., or 1.18 D., is the effect in the average woman during her two and one-half years of menopause. This is based on the assumption that it takes less than two and one-half years for the average woman to get over the effect of menopause. The average woman loses more than 1.00 D. of accommodation due to the menopause alone than does the woman of the same age not in menopause. In looking over my records, I noted that individual women, during the first two and one-half years after the beginning of menopause, lose about 1.00 D. more of accommodation than do men for the same ages. Similar changes were noted for the artificial menopause. This demonstrates the necessity for frequent changes in glasses in women who are passing through the menopause.

OLD AGE

In the study of the old age group (above 69 years) I called the eyes healthy if there was no pathologic condition or cataract and if vision was above 5/60. I classified cataract as incipient when vision was 5/10 or better, as premature when vision was 5/10 to 5/60 and as mature when vision was 5/60 or below. Eyes with other diseases were classified as seeing when vision was 5/40 or better and as blind when vision was 5/60 or below. This classification was made for statistical purposes only. For statistical purposes, also, I assumed that light perception equaled 1/500, instead of 5/infinity, because I could not average infinity with definite figures.

8. Fuchs, E.: Textbook of Ophthalmology, authorized translation from the twelfth edition, revised and greatly enlarged, by Alexander Duane, Philadelphia, J. B. Lippincott Company, 1919, p. 860.

9. Novak, E.: Textbook of Gynecology, Baltimore, Williams & Wilkins, 1944, p. 114.

In the old age group (70 to 80 years), of 1,404 eyes studied, 253 (18 per cent) had healthy eyes and clear lenses, and 846 (60.2 per cent) cataractous lenses; 13.6 per cent (eyes with other diseases) were classified as seeing, and 9.3 per cent, as industrially blind. The average vision of eyes with healthy, clear lenses was 5/7.5.

EXTREME OLD AGE

No one was found with clear lenses after 87 years of age. Of 236 eyes of persons between the ages of 81 and 87, only 19, or 8.0 per cent, were healthy eyes with apparently clear lenses. At 80 years of age all can expect to have senile cataracts.

It should be noted that the entire curve of refraction, from birth to old age, includes only those eyes that were healthy with clear lenses. Since most eyes after the age of 70 have senile cataracts, the eye of old age becomes more myopic each year, in spite of the fact that a few lenses appear to be clear. Hence, this myopic curve continues until 87 years of age, after which my statistics are of no value, owing to the limited number of cases.

SENILE CATARACT

Since senile cataract affects the refraction and vision of later life, a special study was made of persons in this age group. For statistical purposes, it is assumed that all senile cataracts occurring after the age of 40 were senile cataracts. The senile cataract group before the age of 40 was classified as presenile.

A study of my series of 1,850 senile cataracts occurring after the age of 40 gave the following data:

Age	Number of Senile Cataracts	Average Vision Seeing Eye	%	Average Vision Industrial Blindness	No.	Average Vision Aphakic Eye	No.
40-47	80	5/11.2	66	1/125.6	27	5/5.3	5
48-57	182	5/16.1	59	1/143	76	5/19.5	11
58-67	483	5/15.6	79	1/151.5	93	5/14.6	41
68-77	785	5/19.8	83	1/209	120	5/30.6	137
78-87	320	5/30.1	79	1/244	68	5/33.3	46
					384		240

$$\text{Total } \frac{1,850}{2} = 925 \text{ center of group, 69 years 9 months of age.}$$

In this study the vision of seeing eyes with senile cataract is compared with the vision of seeing aphakic eyes.

In a local hospital (St. Joseph's Infirmary), of 320 operations for senile cataract, covering a period of four years, the average age of the patients at the time of operation was 66½ years. Only 20 of these patients, or 6.2 per cent, were past the age of 80, indicating that many

extremely old people are not operated on for cataracts causing blindness, a deplorable fact. An operation would better the vision of many of these persons during the last years of their lives. Statistically, these figures mean that the average age for cataract operation (66½ years) does not indicate the average age that a person can expect to have cataract (69¾ years). More old people should have operations for cataract.

PROGNOSTIC SIGNIFICANCE

To get the ideal refraction for any age below 31, 0.610 D. is subtracted from the age norm for that year; e. g., + 3.610 D. (the age norm for 9 years) — 0.610 D. = + 3.00 D., the ideal refraction for a child 9 years of age.

Static emmetropia in the young is not the ideal refraction except near the age of 31. Emmetropia at the age of 7 years means that the child will have about — 2.00 D. of myopia at the age of 15. The outlook for senile cataract may be stated as follows: After the age of 40 a myopic change of a ½ D. or more in less than a five year interval probably means incipient cataract. A stationary refraction over a period of five years suggests that no cataract will develop for a few years. A hypermetropic change of ⅓ D. or more after the age of 40 means no senile cataract for many years.

VISION

Chavasse [10] stated that the vision of the average infant at 4 months of age is 6/768 (1/128); at 6 months, 6/288 (1/48), and at 9 months, 6/72 (1/12). My yearly averages for visual acuity are as follows: 1 year of age, 5/35 (estimated); 2 years, 5/12.1, and 12 years, 5/5. The E chart was used with children from 2 years of age until they entered the fourth grade in school.

This visual acuity increases until the age of 18, when it reaches a maximum of 5/4.4. It remains stationary until the age of 62, when it drops to 5/5.2. From 62 to 69 it parallels the refractive curve until 70, when it has a more sudden drop, due to senile changes in the eye, including cataract.

Since at the age of 69 years 9 months the average person has cataract, it would not be statistically fair to exclude the vision of many persons with incipient cataract who still have useful vision. Therefore, beginning at the age of 70, I have charted the visual acuity of all persons with healthy eyes and of persons with incipient cataract having vision of 5/40 or better. This is shown in the graph.

This curve of vision is a much fairer curve and is much more regular than the upper curve on the graph. The reason that vision is better from

10. Worth, C.: Worth's Textbook on Squint, edited by F. B. Chavasse, Philadelphia, P. Blakiston's Son & Co., 1939, p. 105.

70 to 80 years of age in the group with clear lenses is because so many eyes with incipient cataracts at this age are represented in the lower curve. After 80 years of age the vision is about the same in each curve, because practically all eyes show nuclear changes with the slit lamp even though the lenses have been classified as clear.

PERCENTAGE OF 5/5 OR 20/20 VISION

The percentages of all eyes with healthy clear lenses from birth to 69 years which had vision of 5/5 or better are charted on the lower curve. Vision of 5/5 was first found at the age of 3 years, at which age its incidence was 3 per cent, at 4 years it was 8 per cent, and at 5 years, 22 per cent with gradual increase until 22 years, when it was 94 per cent. Vision remained fairly constant until the age of 62, when it began to drop, probably owing to beginning senile changes in a few cases. E. Marks (Berens [11]) found that 16 per cent of children at 3 to 4 years had 20/20 vision, a percentage which is much higher than was my experience.

The average age for senile cataract is 69 years 9 months. Therefore, after the age of 69 many of the people who have 5/5 vision may have beginning cataract. Hence, after the age of 70, cases of incipient cataract were included in the lower curve on the graph. This accounts for the sudden decrease in vision from the age of 60 to that of 70.

In a study of the vision of the aphakic eyes in persons past 60, it can be seen that the loss in vision declines at about the same rate as that in eyes with fairly clear lenses. This loss of vision is due to the senile changes back of the lenses, and vision cannot be restored to the vision of youth or adult manhood even by a perfect operation.

The age factor in refraction and vision plays a large part in the daily practice of every ophthalmologist. It can truly be said that in regard to vision the old reach their second childhood. The average vision of healthy eyes with clear lenses for the age of 87 is about the same as that for a child of 1½ years.

Following the suggestion of Dr. Edward Jackson,[1] I made this study of the age norms of refraction and vision. It is hoped that ophthalmologists who have enjoyed a larger practice will add to and correct these statistics. There have been many other ophthalmologists with a larger number of records, better qualified than I, who could have made this study. Since they have not done so, I offer this paper.

CONCLUSIONS

The average static refraction at birth is + 2.32 D. (Herrnheiser [8]) The hypermetropic change of early childhood to the age of 7 years is

11. Berens, C.: The Eye and Its Diseases, Philadelphia, W. B. Saunders Company, 1936, p. 174.

+ 1.617 D. The axial myopic change of the young (8 to 30 years) is — 3.327 D.; the hypermetropic change of middle age (31 to 64 years), + 1.362 D., and the senile myopic change (65 to 87 years), — 2.367 D. Average vision is 5/35 at 1 year of age; 5/12.1 at 2 years and 5/5 at 12 years. It reaches the maximum 5/4.4 at the age of 18 and remains stationary until 62, when it drops to 5/5.2. At the age of 70 it makes a sudden drop, owing to senile changes in the eye.

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ABSTRACT OF DISCUSSION

DR. ALFRED COWAN, Philadelphia: The material presented by Dr. Slataper represents an immense amount of work, and he deserves great credit for his patience, industry and intellectual interpretation of the data. A paper of this kind also requires courage, because so many factors are concerned that probably nine out of ten ophthalmologists will take exception to, or find fault with, certain procedures or methods of examination or the analysis of the findings.

I, for instance, find fault with the universal use of the so-called spherical equivalents. As I have often stated before, one may say that quantitatively a cylinder of a given power is equivalent to one-half the same given power of a spherical lens; qualitatively, however, there is no such equivalence. A 4 D. cylinder can never be properly replaced by a 2 D. sphere, nor can a plano lens be substituted for a — 3 D. sph. ⌢ + 6 D. cyl. In my opinion, the so-called equivalent power may be used as a measure of compound hypermetropic or myopic astigmatism in the way in which it is used here by Dr. Slataper, but not as a measure of mixed astigmatism.

A condition that should be applied to any investigation seeking to establish norms is that the material represent a cross section of the whole population, a true picture of the general state, not merely that of a number of office and clinic patients who seek relief from discomfort, often the result of an uncorrected refractive error. The vast majority of persons under 40 or 45 years of age with emmetropic, or nearly emmetropic, eyes and those with low or medium degrees of hypermetropia are never seen by an ophthalmologist. Dr. Slataper's statistics tend toward the inclusion of too great a number of persons with myopia, astigmatism and high grade hypermetropia in proportion to the population. Hypermetropia, even fairly high grade hypermetropia, especially in very young persons, is more prevalent than the available statistics indicate.

It is interesting that Dr. Slataper found, with Dr. E. V. L. Brown, that the refraction decreased (hypermetropia increased) in children up to 7 years of age and that the figures of these two investigators are so close. Is it possible that there might be a different picture if all children, and not chiefly patients, were examined? If the normal trend is toward a decrease in the refraction up to 7 years of age, as shown, it seems that the same should be found in children with myopia; that is, myopia should decrease up to 7 years of age.

The decrease in refraction (increase in hypermetropia) between the ages of 31 and 64 may well be accounted for by the relaxation of the

accommodation as age increases, or, as Straub and Falkenburg stated, by loss of tone in the ciliary muscle.

Among the many interesting points which Dr. Slataper has brought out is the influence of the menopause on the loss of accommodation. I agree with him that in general the loss of accommodation is more rapid and occurs at an earlier age in women than in men, but this loss gradually slows down until in the early fifties, and thereafter, the power of accommodation for men and that for women of a given age are about the same.

Dr. Everett L. Goar, Houston, Texas: This paper represents a tremendous amount of work and is a valuable contribution to ophthalmic literature. I know of no one else who has had the patience and endurance to review over 35,000 refraction records and to publish the findings.

I shall not attempt to discuss Dr. Slataper's tabulations showing the annual age variations in refraction. Statistics are likely to make a person dogmatic in certain statements. I recognize that all life insurance companies base their rates on actuarial statistics; but, in addition, they also look very carefully at the individual patient, and if he deviates from the normal they "rate up" the applicant. Dr. Slataper makes the statement that "emmetropia" at the age of 7 years means that the child will be myopic at the age of 15. Statistically this statement is correct, but in individual cases it may be quite wrong. It is true that an ophthalmologist likes to see 1 or 2 D. of hypermetropia in a young child as a buffer against myopia and that he should warn the parents to have the eyes examined frequently in order to detect the myopia early if it appears. I have followed many such children to adult life who were close to emmetropia at 7 or 8 years of age, and they have never become myopic. On the other hand, I have seen children with over 3.00 D. of hypermetropia who became myopic before adult life. I believe that myopia is usually familial and that no treatment has the slightest effect on it. I cannot subscribe to the statement frequently heard that myopic eyes may be as healthy as hypermetropic eyes. If that is true, there should be as many hypermetropic patients with changes in the vitreous and retinal separation as there are myopic patients; that is not the case.

It has been my understanding that in older persons the tendency toward hypermetropia or myopia depends on what happens to the crystalline lens. Swelling of the lens and sclerosis of the lens produce myopia, while flattening produces hypermetropia. As a person grows older, if the lens flattens as it scleroses, the processes may neutralize each other and the refraction remain about the same. If, however, the sclerosis is intense and the lens does not flatten, but may even increase along its anteroposterior axis, lenticular myopia occurs, and the patient receives the doubtful boon of "second sight."

I know of nothing in ophthalmology that requires better judgment than the question of operation for cataract in very old people. Dr. Slataper deplores the fact that only 6.2 per cent of persons with cataract over 80 were operated on. I am inclined to believe that this proportion is about right. I do not mean that people should be allowed to go blind because they are old. Many elderly people who have intense nuclear sclerosis may have very poor distance vision; but with a good light they can read well without glasses, and they have the great advantage of

binocular vision. One should consider very carefully before subjecting such a person to a cataract operation, lest his last state be worse than the first. I have carried many of such elderly persons along without operation until death solved the problem. In my earlier days I operated on some of them, to my profound regret.

DR. F. J. SLATAPER, Houston, Texas: I wish to thank Dr. Cowan and Dr. Goar for their discussion of this paper. I am satisfied with the statistical value of my "norms of refraction from birth to old age" and with the "norms of vision" from birth to 64 years of age. However, since the curve for senile myopia starts for patients at the age of 65, owing to the beginning of cataract in many cases, and my average age for senile cataract was found to be 69 years 9 months, I believe that my norms of vision for persons past 65, and especially past 70, are not correct, owing to the fact that I excluded all eyes with cataract. The normal vision of old age must include values for all seeing cataractous eyes, since most of the eyes in this age group have cataract.

The last eleven years in this series averaged only 12 cases for each year, because most of the patients at this age had cataract. I hope in the future to present a supplementary report giving the vision for each age of all healthy eyes as corrected with lenses, including cataractous eyes with useful vision in persons from 65 to 95 years of age.

THE EYE IN TERATOMAS

Report of a Case and Review of the Literature

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NEW YORK

TERATOMAS have been the subject of innumerable scientific and philosophic speculations since the inception of oncology. Their bizarre disorganization of structure and their even more bizarre approach to organogenesis have long aroused great interest among pathologists and embryologists.

Teratoma, literally a wondrous or monstrous growth, may be defined as a tumor containing tissues derived from two or more germ layers. Most body tissues have been described in these tumors, and it has been said that the teratoma may well serve for a review of histology.[1] Characteristically, however, gonadal tissues are hardly ever seen, and certain other tissues, such as liver, very rarely. Skin, bone, cartilage, connective tissue elements, epithelium of the respiratory and gastrointestinal tracts, smooth and striated muscle and glial and nerve tissues may all be present in abundance. These tissues may be mature or immature, the latter constituting the malignant, embryonal teratoma; but even the adult tissues may undergo malignant change, with subsequent metastases. At best, the borderline between the immature and the mature type is vague. The common dermoid cyst is a teratoma in which elements of the skin and its appendages predominate, although careful search will usually reveal nonectodermal elements as well. Willis[2] expressed disapproval of the term dermoid with reference to teratomatous cysts, reserving it exclusively for inclusion cysts of body surface ectoderm.

Teratomas may occur anywhere in the body but are most frequently observed in the gonads. They occur in the eye and its adnexa, usually as a dermoid cyst or a dermolipoma, and rarely as a solid orbital teratoma.

From the Departments of Ophthalmology and Pathology, Beth Israel Hospital.

Presented at a meeting of the New York Academy of Medicine, Section of Ophthalmology, Oct. 18, 1948.

1. Moore, R.: Textbook of Pathology, Philadelphia, W. B. Saunders Company, 1944, p. 1119. Foote, N.: Pathology in Surgery, Philadelphia, J. P. Lippincott, 1945, p. 384.

2. Willis, R. A.: A Further Study of the Structure of Teratomata, J. Path. & Bact. **45**:49, 1937.

The attempts at organogenesis so often noted in solid teratomas range from histologically identifiable segments of intestine to extremely rare structures resembling a malformed human body (Plaut [3]). It is not surprising, therefore, that the eye should be represented in varying degrees of differentiation in these peculiar tumors. The ability of these tumors to elaborate organs or organoid structures does not appear to be altered by the site in which they grow. Thus, optic anlages have been noted in teratomas of the ovary, testis, buttock, sacrum, urinary bladder, kidney, abdominal cavity, intestine, thyroid, cranium, orbit and pituitary gland and doubtless may be found wherever else the tumor occurs.

The classification of teratomas is unsatisfactory, owing to ignorance of their histogenesis. Numerous theories of origin have been proposed: (1) proliferation of dislocated or supernumerary blastomeres; (2) parthenogenesis of gonadal or extragonadal germ cells; (3) internal twinning; (4) growth of fertilized polar bodies; (5) developmental errors in the primitive streak and early axial structures; (6) organizer activity. Full discussions of these controversial theories are to be found in the papers of Willis,[4] Nicholson,[5] Krafka [6] and Plaut.[3] Theories 1, 2 and 6 are most widely regarded today.

The occurrence of teratomas in the eye and orbit is well known to ophthalmologists, but the presence of ocular structures and adnexa in teratomas arising in other organs of the body has not previously been described in the ophthalmic literature. Such a case and a review of the literature are presented.

REPORT OF CASE

D. W., a white girl aged 19, a virgin, was admitted to Beth Israel Hospital, on Aug. 6, 1947, with a diagnosis of cyst of the right ovary. Her left ovary had been removed four years previously for a dermoid cyst.

Laparotomy was performed, and an encapsulated mass in the right ovary was resected. The pathologic diagnosis was malignant teratoma. Supravaginal hysterectomy with bilateral salpingectomy and removal of the right ovary was performed. The patient received radiation therapy and was discharged on September 24. Her subsequent course has been uneventful.

Gross Description of Specimen.—The specimen was an ovoid cystic tumor measuring 20 by 15 by 9 cm. and containing small solid portions. No anatomic landmarks could be recognized on the outside. On incision, a large amount of thin,

3. Plaut, A.: Dermoid Cyst of an Ovary Containing a Structure Similar to a Human Body (Homunculus), J. Mt. Sinai Hosp. **12**:567, 1945.

4. Willis, R. A.: (*a*) Structure of Teratomata, J. Path. & Bact. **40**:1, 1935; (*b*) footnote 2.

5. Nicholson, G. L.: Studies on Tumor Formation, Guy's Hosp. Rep. **84**: 140 and 389, 1934; **85**:8 and 379, 1935.

6. Krafka, J., Jr.: Teratoma: An Explanation of Its Cause Based on the Organizer Theory of Embryology, Arch. Path. **21**:756 (June) 1936.

dark brownish fluid escaped. About one-third the volume of the mass was soft—partly solid and partly microcystic. A small, flat portion near the periphery was bony.

Microscopic Description.—There was a great variety of mature and immature tissues. Various types of cartilage and bone were abundant. A number of optic rudiments were present.

Optic Rudiments: Neuroepithelium, in the form of tubules, masses and small cysts, was present in abundance. In one place a small irregular cyst lined with

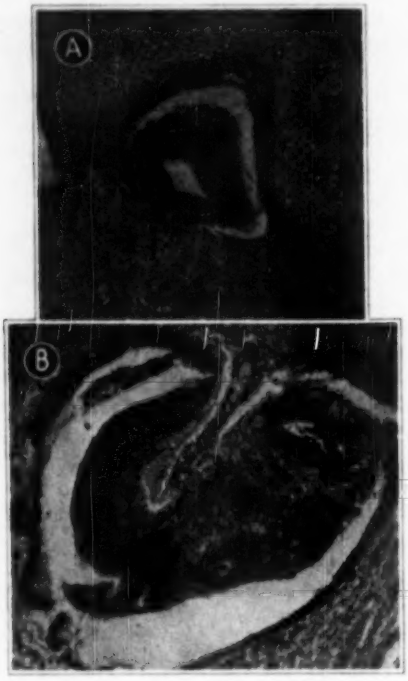

Fig. 1.—*A*, distorted optic anlage; × 65. *B*, optic anlage approximating the 15 mm. stage; × 100.

a thick mantle of neuroepithelium with deep blue-staining nuclei was contiguous to a compressed, oval, cystlike layer of low cuboidal cells filled with yellow-brown pigment granules (fig. 1 *A*). In another place was a mass of fragmented, disorganized neuroepithelium, partly tubular, partly cystic, showing many rosettes, areas of necrosis, small hemorrhages and a very irregular strip of pigment epithelium. Besides these extremely distorted vestiges, there was a rudimentary eye which had achieved a considerable degree of differentiation, exhibiting at the same time several remarkable structures (fig. 1 *B*). It had the appearance of the double-walled, secondary optic vesicle (optic cup) at about the 15 mm. (5 to 6 week) stage of the

normal embryonic eye. Curiously, only half the eye showed orderly development. In the other half the outer wall was slightly less mature, and the inner wall was strikingly undifferentiated and disordered.

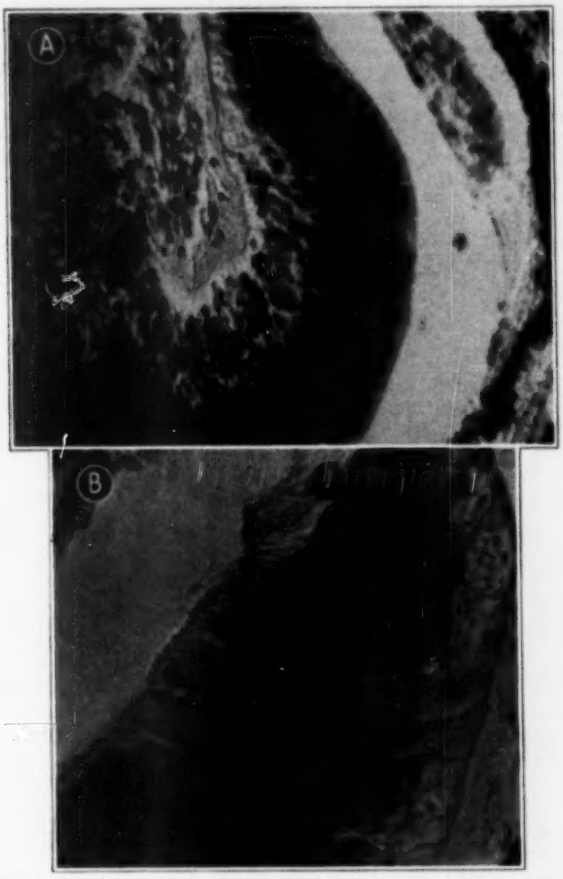

Fig. 2.—*A*, well developed half of optic anlage; × 300. *B*, anterior lip of well developed half of retina; × 750. Note mitotic figure and fibrils.

The outer wall was composed of pigmented, polygonal cells with oval to round, vesicular nuclei, each containing a nucleolus. The nuclei of the less mature half appeared to be arranged in two to three rows, although, as suggested by Mann[7]

7. Mann, I.: The Development of the Human Eye, London, Cambridge University Press, 1928.

for the normal eye, this may have been due to a difference in level, each cell actually extending from surface to surface. The basement membrane bordering the primary cavity of the vesicle had an indistinct, fuzzy edge, suggestive of cilia. Occasional mitotic figures were seen among the nuclei near the lumen. Pigmentation was patchy in this half. The nonpigmented cells were taller than the well pigmented, low cuboidal cells of the more mature portion. The oval, yellow to deep brown pigment granules occurred throughout the cell but were more numerous toward the lumen. In places they lay free in the adjacent tissue.

The outer wall became free from pigment and thicker toward the anterior end, where it invaginated to form the inner wall of the retina. It continued to widen as it extended backward, encroaching on the cavity of the primary vesicle. A tonguelike process of loosely aggregated nuclei extended into the cavity from the anterior lip of the cup.

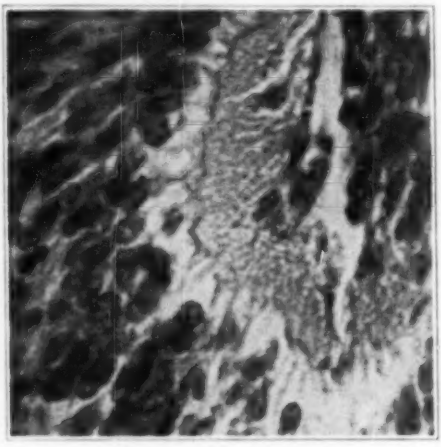

Fig. 3.—Detail of vitreous, internal limiting membrane and fibers of Müller; × 750.

The well differentiated half was composed chiefly of cells with oval, vesicular nuclei, each containing a nucleolus, and oriented perpendicularly to the basement membrane (fig. 2 *A*). The basement membrane was separated from the nuclei by a narrow, clear space traversed by delicate fibrils. It was lined with short, matted protuberances, which in places were suggestive of cilia. A number of mitotic figures occurred among the nuclei near it (fig. 2 *B*).

The nuclei of the inner wall were separated by a narrow interval into an outer, basal layer and an inner, superficial layer. The basal layer, containing seven to eight rows of oval nuclei, corresponded to the outer neuroblastic layer of the embryonic eye. The narrow, clear interval, relatively free of nuclei and traversed by many fine fibers, corresponded to the transient fiber layer of Chievitz. The superficial layer, only four to five nuclei wide, corresponded to the inner neuroblastic layer. A number of the latter nuclei were round and suggested cell bodies, although nerve processes were not definitely discernible; hence, it cannot be said

that they actually represented ganglion cells. In the deeper portions of this layer occurred cells with oval nuclei, from the extremities of which fibers passed outward through the transient layer and inward through another clear interval corresponding to the nerve fiber layer, to end in an expansion on a definite internal limiting membrane. These corresponded exactly to fibers of Müller and terminated in identical footplates. The internal limiting membrane had a slightly scalloped appearance, possibly due to traction exerted by the fibers on fixation (fig. 3).

The homologous features of retinal structure in the human embryonic eye and in the teratomatous eye are summarized in tables 1 and 2 (normal values from Mann,[7] figs. 70 and 71 and p. 104). From the foregoing data, the stage of development of the teratomatous eye can be placed at about 15 mm. (5 to 6 weeks). The approach to normality in one part of this eye is all the more striking in view of the extreme abnormality of the other.

TABLE 1.—*Homologous Features of the Embryonic and the Teratomatous Eye*

Embryonic Eye	Teratomatous Eye
1. Basement membrane, ciliated	1. Basement membrane with suggestive cilia
2. Outer neuroblastic layer (6-8 rows)	2. Basal layer of nuclei (7-8 rows)
3. Fibers of Müller	3. Oval nuclei with fibrous processes ending in footplates
4. Transient layer of Chievitz	4. Clear area traversed by fibers
5. Inner neuroblastic layer	5. Inner nuclear layer (ganglion cells?)
6. Nerve fiber layer (mostly Müller's fibers)	6. Clear area traversed by fibers from 3
7. Internal limiting membrane	7. Internal limiting membrane

TABLE 2.—*Measurements for 12 and 17 Mm. Stage of Embryonic Eye and Teratomatous Eye*

	17 Mm. Embryonic Eye	Teratomatous Eye	12 Mm. Embryonic Eye
A. Total width inner wall of optic cup....	0.175 mm.	0.140 mm.	0.105 mm.
B. Width of original marginal layer (7-4)..	0.08 mm.	0.06 mm.	0.048 mm.
C. Ratio B/A.....	0.45	0.43	0.45
D. Diameter of pigment epithelium layer..	0.02 mm.	0.02 mm.	0.02 mm.
E. Over-all diameter of optic cup.....	0.7 x 0.7 mm.	0.6 x 0.6 mm.	

Immediately beyond the internal limiting membrane, intimately in contact with it and occupying the depth of the cavity of the cup was a mass of colorless, refractile granules with a slightly fibrillar appearance, which apparently represented vitreous (fig. 3). Adjacent to it, occupying most of the cavity down to the internal limiting membrane, was a columnar condensation of mesenchymal cells containing red blood cells in vascular spaces. It was an obvious homologue of the hyaloid artery. Several vascular buds lay on the vitreous. A number of capillaries and an occasional pigment-containing cell lay adjacent to the outer surface of the pigment epithelium, completing the resemblance to the uveal tunic. There was no trace of lens or optic nerve.

The abnormal half of the inner layer presented clumps and tubes of intensely staining, completely undifferentiated neuroepithelium, showing many nuclear abnormalities, mitotic figures and staining and cytologic variations (fig. 4). A few true rosettes (average diameter, 0.04 mm.) were seen here and were present in larger numbers elsewhere in the section (fig. 5*A*). A typical rosette consisted of a layer

of cells several nuclei in width, surrounding a clear central lumen. A rim adjacent to the lumen was free of nuclei and was traversed by fine fibrils, ending in a basement membrane, from which cilia-like processes arose. Occasionally one could

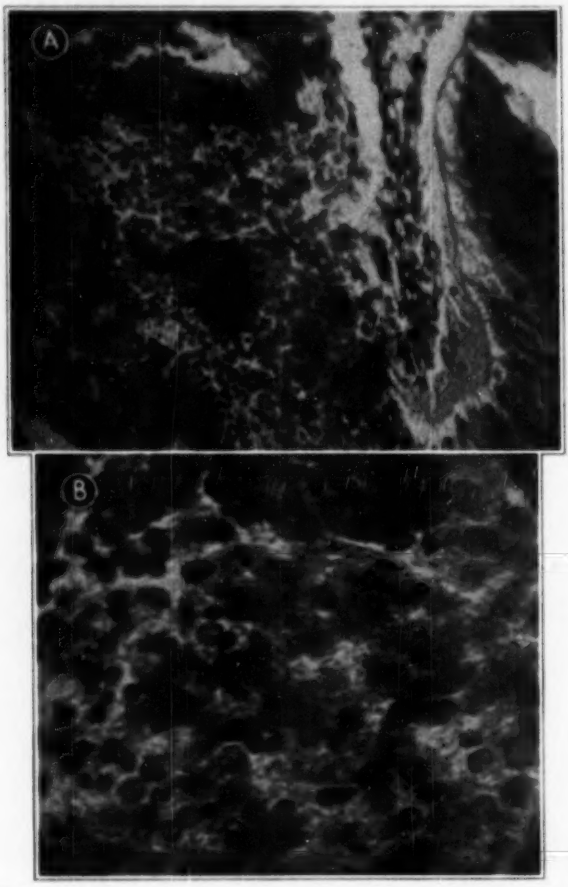

Fig. 4.—*A*, abnormal half of optic anlage resembling neuroepithelioma; × 300. *B*, detail of abnormal half of retina; × 750.

see a few fibrils lying within the lumen. Both round and horseshoe-shaped rosettes occurred (fig. 5 *B*). The transition from normal to abnormal retina was abrupt, and the histologic appearance of the latter closely resembled that of malignant neuroepithelioma retinae arising in the normal eye.

REVIEW OF LITERATURE

Teratoma of the Sex Glands.—The earliest significant report of eyelike structures in teratomas was published by Verneuil[8] (1855), in a series of papers entitled, "Inclusion scrotale et testiculaire." He cited

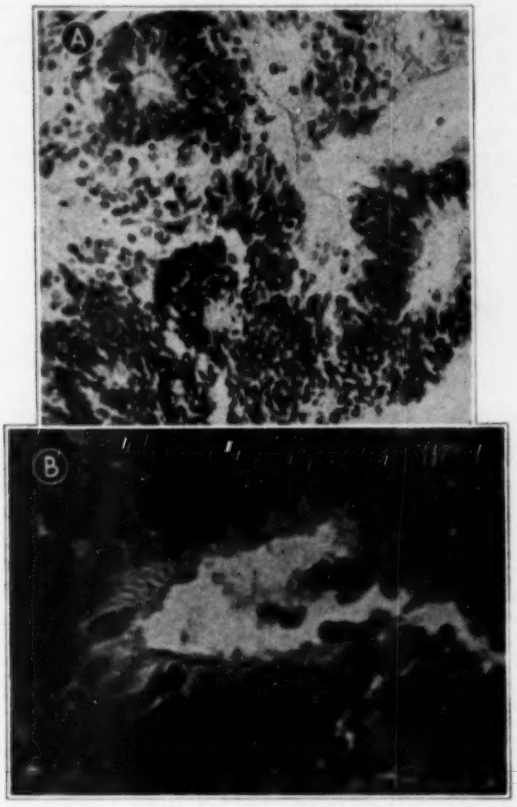

Fig. 5.—*A*, rosettes; × 500. *B*, horseshoe-shaped rosette; × 750

Saint-Donat (1696), who described a massive teratoma of the testis containing a bony globe in the shape of a skull. This bony mass presented two orbit-like cavities enclosing black vesicles lined with a uveal

8. Verneuil, A.: Inclusion scrotale et testiculaire, Arch. gén. de méd., 1855, vols. 1 and 2.

tunic and containing a "flowing lymph," which he called aqueous humor. In his own case of a teratoma of the testis, Verneuil described a cyst containing pigment epithelium arranged partly in typical mosaic form and showing all the characteristics of the pigment epithelium of the eye.

Marchand[9] (1881) was the first to describe an ovarian teratoma containing small cavities lined with pigment epithelium like that of the retina, which was visible grossly as intensely black flecks.

Baumgarten[10] (1887), unaware of Marchand's work, stated that he was the first to describe a dermoid cyst of the ovary containing eyelike formations. These were paired or multiple; one was a delicate, transparent vesicle arched like a cornea above, which allowed a dark, pigmented membrane, resembling the tunica uveae, to show through. Outside the latter was a loose connective tissue containing vessels, establishing the likeness to choroid. The author stated that the pigment epithelium was none other than the outer layer of the secondary optic vesicle, and, since pigment epithelium occurred nowhere in the body but the eye, the structure must be considered as such. The pigment particles were dark brown, round granules, spindle shaped or in crystalline bars. Actual retina was not observed, nor was there any trace of optic nerve. Cerebral tissues were closely associated with the anlage, surrounding it and lying within the cavity.

Kappeler[11] reported the presence of retinal pigment epithelium in dermoid cysts. Such areas were macroscopically visible as shiny, black spots lining the inner surface of small clefts. Microscopically, the pigment epithelium, resting on connective or nerve tissue, appeared as typical, hexagonal cells, arranged in a mosaic.

Pigmented structures considered analogous to optic anlages were reported in ovarian teratomas by Saxer[12] and Krömer.[13] Three cases of such structures in teratomas of the testis were cited by Wilms,[14] as well as in ovarian dermoids.[15] The earliest American contributors were Lovett and Councilman[16] who observed cysts with an outer wall of

9. Marchand, F.: Ueber eine grosse teratoide Mischgeschwulst des Ovariums, Breslau. ärtzl. Ztschr. **3**:249, 1881.

10. Baumgarten, P.: Ueber eine Dermoidcyste des Ovarium mit augenähnlichen Bildungen, Virchows Arch. f. path. Anat. **107**:515, 1887; **108**:216, 1887.

11. Kappeler, F.: Inaug. Dissert., Zurich, 1896, cited by Miller.[01]

12. Saxer, F.: Ein Beitrag zur Kenntnis der Dermoide und Teratome, Beitr. z. path. Anat. u.z. allg. Path. **31**:452, 1902.

13. Krömer, P.: Ueber die Histogenese der Dermoidcystome und Teratome des Eierstocks, Arch. f. Gynäk. **57**:322, 1899.

14. Wilms, M.: Die teratoiden Geschwulste des Hodens, usw., Beitr. z. path. Anat. u.z. allg. Path. **19**:233, 1896.

15. Wilms, M.: Ueber die Dermoidcysten und Teratome mit besonderer Berücksichtigung der Dermoids der Ovarien, Deutsches Arch. f. klin. Med. **55**:289, 1895.

16. Lovett, R., and Councilman, W.: A Case of Double Teratoma, J. Exper. Med. **2**:427, 1897.

pigmented epithelium and an inner wall of nonpigmented neuroepithelium in a teratoma of the testis in an infant. After resection of this tumor a fatal intracranial teratoma developed.

Another American, Montgomery,[17] described a teratoma in the testis in a newborn infant which contained a flattened cyst partly covered with pigmented cells. On the opposite wall, and in places connecting with the pigmented layer, was a formation of neuroepithelium closely resembling retina. Its deep surface was lined with projections not unlike the cones of the retina. Layers of oval nuclei, from two to three in depth, resembled the granular layers. Montgomery reviewed the literature, citing 16 cases in which pigment epithelium had been reported.

Ocular adnexa were reported in dermoid cysts: an eyelid with lashes, Graves [18]; a fully developed upper lid and a partly developed lower lid with a vesicle (eye) between, as well as lashes and brow, Habs [19]; a lid with follicles, cilia and other structures, near a cleft lined with pigment epithelium, Kartuschanskaja.[20]

Katsurada [21] described optic anlages, often paired, in 3 dermoid cysts. These anlages consisted of cavities lined with pigment epithelium. One contained a round, almost homogeneous body, 85 microns in diameter, which was likened to vitreous. His descriptions, curiously, are almost identical with those of Baumgarten, who was not cited in his paper.

Hirst,[22] at a meeting of the College of Physicians in Philadelphia, presented a specimen of dermoid cyst with an eye, stating, "It is one of the most curious errors of anatomical structure that can be seen." Unfortunately, there was no further gross or microscopic description. A comparable event was the presentation at a German gynecologic society of a "dermoid cyst with a distinctly rudimentary optic anlage" by Amann [23].

Askanazy [24] noted the not infrequent occurrence of optic anlages in ovarian dermoids. Retinal pigment epithelium was sometimes arranged in lamellas, sometimes in clumps, or was of the most varied and anomalous forms. Similar observations were made in teratomas of the testis.[25]

17. Montgomery, D. W.: A Teratoma of the Abdominal Cavity, J. Exper. Med. **3**:259, 1898.

18. Graves: M. Progress, February 1893; cited by Askanazy.[24]

19. Habs: Ovarialdermoidcyste, München. med. Wchnschr. **47**:1789, 1900.

20. Kartuschanskaja, J.: Inaug. Dissert., Zurich, 1906; cited by Miller.[91]

21. Katsurada, F.: Zur Lehre von den sogenannten Dermoidcysten odor Embryomen des Eierstocks, Beitr. z. path. Anat. u.z. allg. Path. **30**:179, 1901.

22. Hirst, B. C.: Dermoid Cyst with an Eye, Am. J. Obst. **48**:112, 1903.

23. Amann, J.: Dermoidcystom mit deutlicher rudimentärer Augenanlage, Zentralbl. f. Gynäk. **34**:1636, 1910; Monatsschr. f. Geburtsh. u. Gynäk. **33**:243, 1911.

24. Askanazy, M.: Die Dermoidcysten des Eierstocks, Stuttgart, Bibliotheca Medica, 1905, pt. C, no. 19.

25. Askanazy, M.: Die Teratome nach ihrem Bau, Verhandl. d. deutsch. path. Gesellsch. **11**:39, 1907.

Unpigmented neuroepithelium was encountered in the inner wall of optic cups formed in teratomas. He stated that chromatophores of the choroid are not characteristic of the eye, since they occur rather constantly in the meninges of the central nervous system.

Ohkudo,[26] in a comprehensive review of embryomas of the testis, cited the cases of Senftleben (page 516), Schwarz (page 528) and Pepere (page 534), in which pigmented retina was observed. He presented several instances (cases 8 and 12) of optic cup formation.

Ribbert [27] described an ovarian teratoma containing a thin-walled cyst the size of a nut, which appeared to be a rudimentary eye. A broad nerve containing numerous ganglion cells extended into the wall of the cyst like an optic nerve.

Heijl,[28] who presented an exhaustive study of teratomatous optic anlages, described an unusual dermoid cyst containing an unquestionable optic organ. This consisted of a flattened, compressed, vesicular or tubelike formation. Its inner wall was formed by a partly smooth, partly folded, strongly refractile membrane, consisting of parallel connective tissue fibers with few nuclei. He stated that there is no structure in the body like this but the cornea. It continued into vascular connective tissue and a pigment epithelial layer. No pars optica retinae or optic nerve was seen. He noted, in summary, that dermoid cysts may contain definite, macroscopic visual organs, lids and rudiments consisting of tunica externa, tunica media, pigment epithelium and, occasionally, lenses. Although cysts with pigment epithelium were frequently seen in dermoids, no optic retina was discovered.

In solid teratomas (cases 23 and 26) Heijl found numbers of pigment formations, varying in development from simple neuroepithelial tubes to well differentiated optic cups. Several structures resembled the ciliary body. Many fragmented anlages were observed in this group. It is interesting to note the structural variability of rudiments of the eye in these nearly always malignant tumors. Heijl reported malignant neuroepithelial growths in teratomas which corresponded exactly to those occurring in the mature eye. In a few instances he observed malignant melanomas arising from embryonal tumors of the sex glands. He pointed out the close relation of teratomatous eyes to tumors and developmental anomalies of the eyes.

Rohdenburg [29] reported pigment epithelium and traces of developing retina in 6 of 61 ovarian teratomas.

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26. Ohkudo, S.: Zur Kenntnis der Embryome des Hodens, Arch. f. Entwcklngsmechn. d. Organ. **26**:509, 1908.

27. Ribbert, H.: Geschwulstlehre, ed. 2, Bonn, F. Cohen, 1914, p. 657.

28. Heijl, C. F.: (*a*) Die Morphologie der Teratome, Virchows Arch. f. path. Anat. **229**:561, 1921; (*b*) Ueber rudimentäre Sehorgane in Teratomen, ibid. **271**:670, 1929.

29. Rohdenburg, G. L.: An Analysis of Five Hundred Tumors of the Ovary, J. Lab. & Clin. Med. **12**:211, 1926.

Abadie [30] presented an interesting case of polymorphous embryoma of the testis with metastasis. In addition to many other tissues, it contained neuroepithelial formations, varying from tubules to solid masses with rosettes. Certain of these, by virtue of their architecture and the presence of retinal pigment, represented primary optic vesicles. Others were fragmented, of abnormal shape and lacking in pigment. He stressed the "curious" orientation of the pigment granules toward the lumen of the vesicles, rather than toward the choroid, such as, according to him, occurs in the secondary optic vesicle. (Corsy and associates [31] also alluded to this observation. The feature was also present in the case reported here.) In addition, there were metastases to the left epigastric region consisting of pure, undifferentiated neuroepithelium with many rosettes and nuclear abnormalities.

Corsy, Dome and Plantevin [31] reviewed nearly 100 embryomas of the coccyx, ovary and testis. Retinal structures were seen in 12, in 2 of which they showed malignant change. Their structure was extremely diverse, but some reproduced primary and secondary optic vesicles. Isolated chromatophores were noted in the mesenchyme near the neuroepithelium, a phenomenon that has been mentioned several times in the literature. In 1 of the authors' cases elongated chromatophores were strung out in a long serpentine train. The authors recalled in this connection the proposal of the neurectodermal origin of chromatophores. They concluded that although undoubted optic anlages occur, certain small, isolated or dissociated masses of pigment epithelium did not necessarily represent retina but resulted from a "general pigmentogenous property of neuroepithelium."

Ley [32] described an ovarian embryoma with malignant metaplasia and metastasis of cells of neuroretinal type. The primary tumor contained masses of cells disposed in rosettes with clear centers. Some cells contained pigment. Others were of retinal, choroidal or neuroglial type. Hepatic metastases were composed exclusively of rosettes and the aforementioned cell types, some giving rise to pigmented anlages of the eye. Ley's figure 2 shows a striking resemblance to the classic retinocytoma, arising from the pars ciliaris retinae. A somewhat similar tumor was described by Gosset and Masson.[33]

30. Abadie, J.: Sur un embryome du testicule ayant-donné des métastases neuro-embryonnaires dans la région épigastrique gauche, Compt. rend. Soc. de biol. **92**:98, 1925.

31. Corsy, F.; Dome, H., and Plantevin, P.: Sur l'origine et l'evolution des formations pigmentaires developeés dans les embryomes, Compt. rend. Soc. de biol. **94**:93, 1926.

32. Ley, R.: Embryome á evolution maligne du type retinocytome, Bruxelles-méd. **18**:1514, 1938.

33. Gosset, A., and Masson, P.: Névraxo-épithéliome de l'ovaire, Rev. de gynéc. et de chir. abd. **20**:1, 1913.

The occurrence of metastases of one or several of the component tissues of teratomas has often been noted, as well as malignant change in situ. According to Willis,[3] the malignant property is polyvalent in most testicular and in some ovarian teratomas. No sharp line of distinction can be drawn between benign and malignant teratomas.

Magarinos Torres, Sampaio and Adler [34] reported an ovarian teratoma containing many small cysts lined with discontinuous cubical epithelium (non-neural), histologic examination of which revealed parallel fibers and cells corresponding to those of the lens. The authors suggested that the tumor arose from an area of ectoderm destined to differentiate into the lens.

Intracranial Teratomas.—An epignathus combined with intracranial teratoma containing optic anlages, consisting of two black, pigmented spots, was described by Rindfleisch and Breslau [35] and by Rippmann.[36]

In a similar tumor, Sonnenburg [37] described an eyelid with long lashes, tarsus and conjunctiva but no eye. Saxer [37a] found a teratoma the size of a fist in the third ventricle of an infant. The tumor contained a number of optic anlages, and possibly malignant neuroepithelium with rosette formation. A plexus-like area of neuroepithelium at the anterior end of a cup was suggestive of the pars ciliaris. Ribbert [37b] described a spongioblastoma of the brain containing many rosettes and a number of cysts. One group of cysts was lined with pigment epithelium similar to that of the retina. Another group was lined with a high, cylindric epithelium and contained a homogeneous, slightly striped material, which he considered vitreous. Klapproth [38] observed neuroepithelial cysts in a teratoma of the pineal body. Derman [39] reported a teratoma of the brain in an infant; examination revealed pigmented cystic structures resembling optic anlages. Secondary optic vesicles (cups) were noted by Kraus [40] in a teratoma of the pituitary region. It

34. Magarinos Torres, C.; Sampaio, J. M., and Adler, H.: Teratoma do ovaria com estruturas semelhando cristalino, Mem. Inst. Oswaldo Cruz **35**:181, 1940.

35. Rindfleisch, E., and Breslau: Geburtsgeschichte und Untersuchung eines Falles von Foetus in Foetu, Virchows Arch. f. path. Anat. **30**:406, 1864.

36. Rippmann, E.: Ueber einen bisher nicht beobachteten Fall multipler Intrafötation in- und ausserhalb der Schädelhöhle, Anaug. Dissert., Zurich, D. Bürkli, 1865.

37. Sonnenburg: Ein Fall von Epignathus, Deutsche Ztschr. f. Chir. **5**:99, 1875.

37a. Saxer, F.: Ein zum grossten Teil aus Derivaten der Medulloplatten bestehende grosses Teratom der 3 Ventrikel, Beitr. z. path. Anat. u. z. allg. Path. **20**:399, 1896.

37b. Ribbert, H.: Spongioblastom und das Gliom, Virchows Arch. f. path. Anat. **225**:195, 1918.

38. Klapproth, W.: Teratom der Zirbel combiniert mit Adenom, Centralbl. f. allg. Path. u. path. Anat. **32**:617, 1922.

39. Derman, G.: Zur Kenntnis der Teratom des Gehirns, Virchows Arch. f. path. Anat. **259**:767, 1926.

40. Kraus, E. J.: Ueber ein epignathisches Teratom der Hypophysisgegend, Virchows Arch. f. path. Anat. **271**:546, 1929.

also contained glial tissue, choroid plexus, neuroepithelial tubules and typical small rosettes. Denes [41] published a case of congenital intracranial teratoma probably arising in the vicinity of the left orbit of a stillborn male infant. The left eye was extremely proptosed by the tumor. Histologic study showed tissues of all three germinal layers. Cavities lined with pigment epithelium analogous to retinal anlages were noted, as well as many neuroepithelial rosettes. The latter were described as lined internally by blepharoplasts (his figure 3). These bear considerable resemblance to the rosettes present in my case. Denes commented on the malignant potentialities of this tumor, which, he said, had the microscopic appearance of a pure neuroepithelioma arising in the retina or elsewhere in the nervous system. No other site of tumor was found in the brain or the eyes of the infant.

Intraorbital Teratoma.—Von Hippel [42] reported an orbital teratoma containing many types of tissue in a 5 year old child. An optic anlage presented a curious, inverse arrangement whereby the pigment epithelium layer occurred on the inside and the nonpigmented neuroepithelium layer on the outside. The cavity surrounded by the pigment epithelium contained different types of tissue but no vitreous or lens. He stated the belief that the tumor was entirely analogous to teratoma of the ovary and other organs.

Extracranial Teratoma.—Heijl [28] presented a unique case of a teratoma occupying the right temporal region of a fetus. Several polyps in the tumor contained cysts lined partly with pigment epithelium and partly with nonpigmented neuroepithelium surrounding a clear, slightly fibrillary body called vitreous. He also cited Forster,[43] who observed structures suggestive of eyes in an epignathus.

Sacral Teratomas.—Kümmel [44] (1889) reported the first instance of an optic anlage in a sacral teratoma. It consisted of a cyst, nearly 1 mm. in diameter, formed like a secondary optic vesicle of six weeks' development. The outer layer of simple cubical epithelium was pigmented; the inner, thicker layer was not. He stated that his observations and conclusions were corroborated by Schwalbe.

Spondly,[45] Benno and Schmidt and Schmidt (1891)[46] and Nakayama [47] (1905) described cysts corresponding to primary optic anlages

41. Denes, J.: Intracranial Congenital Teratoma, Am. J. Cancer **40**:329, 1940.

42. von Hippel, E.: Weiterer Beitrag zur Kenntnis seltener Missbildungen, Arch. f. Ophth. **63**:1, 1906; Lubarsch and Henke,[60] 1931, vol. 11, pt. 2, p. 113-114.

43. Forster (1687), cited by Heijl.[28b]

44. Kümmel, W.: Ein Fall von congenital Steisstumor mit augenartigen Bildungen, Virchows Arch. f. path. Anat. **118**:37, 1889.

45. Spondly, O.: Inaug. Dissert., Zurich, 1894; cited by Heijl.[28b]

46. Schmidt, B., and Schmidt, M.: Zwei Fälle von Geschwülsten in der Gegend des Schwanzbeines, Arb. a.d. chir. Univ.-Poliklin. zu Leipz., 1891, vol. 2, p. 15; cited by Spondly.[45]

47. Nakayama, H.: Ueber congenitaler Sacraltumoren, Arch. f. Entwcklngsmechn. d. Organ. **19**:475, 1905.

in sacral teratomas. The cyst in Nakayama's case 13 was more advanced than those in his other 2 cases. It was an optic cup with an outer pigmented layer and an inner nonpigmented layer, the nuclei of which were divided into a thick and a thin zone by a narrow interval of reticular tissue. Thus, the neuroblastic layering of the fetel retina was already evident.

Frank [47a] observed anlages revealing cornea, sclera, ciliary body, pars iridis retinae and choroidal epithelium. Tissues of all germ layers were present. Unfortunately, there were no illustrations. Keller [48] found bizarre formations of pigment epithelium and many neuroepithelial vesicles in a sacral teratoma. Heijl [49b] described 2 sacral teratomas containing a number of anlages, some nearly macroscopic, and many small cysts lined with pigment epithelium and epithelium of the ciliary body.

Abdominal and Intestinal Teratomas.—Klebs [49] described macroscopic anlages of the eye and ear in a fetus-like tumor present in the abdominal cavity of an infant. The mass apparently was associated with the testicular anlage of the host. Pigment epithelium like that of the eye in an abdominal teratoma was mentioned by Pommer.[50] Van Duyse [51] reported a rudimentary eye in a dermoid cyst expelled from the rectum during labor. The eye consisted of a primary optic vesicle connecting through a narrow canal (called the optic peduncle) with a large cavity (called the cerebral vesicle). Projecting into the lumen of the optic vesicle from its pigment epithelium–lined wall near the canal were a number of papillary processes consisting of vascular connective tissue lined with a pigment-free, cubocylindric epithelium. He stated the belief that these represented ciliary processes. Many other notable studies on teratogenesis of the eye were carried out by van Duyse.[52]

Teratomas of the Thyroid.—Pigment epithelium corresponding to that of the retina, arranged in the form of mosaics, lamellas and stripes,

47a. Frank, K.: Zur Kenntnis der congenitalen Sacraltumoren, Deutsche Ztschr. f. chir. **77**:368, 1905.

48. Keller, R.: Zwei Fälle von congenitalem Sacraltumor, Arch. f. Gynäk. **85**:555, 1908.

49. Klebs, E.: Handbuch der pathologischen Anatomie, Berlin, A. Hirschwald, 1876, vol. 1, pt. 2, pp. 1013-1014.

50. Pommer, G.: Teratologisch Mitteilung: Fetale Inclusion im Netze, Ber. d. naturw. med. Versamml. in Innsbruck **18**:116, 1889; abstracted, Centralbl. f. allg. Path. u. path. Anat. **1**:260, 1890.

51. van Duyse, D.: Kyste dermoide (teratoide) avec encephale et œil rudimentaires, Bull. Acad. roy. de méd. de belg. **9**:583, 1895.

52. van Duyse, D.: Éléments d'embryologie et de tératologie de l'œil, Ann. Soc. méd.-chir. d'Anvers **10**:44, 1905.

was described in teratomas of the thyroid by Poult,[53] Hunziker,[54] Ehlers[55] and Russel and Kennedy.[56] Pigment epithelium forming rudimentary optic cups was mentioned by Schönberg.[57]

Teratomas of the Urinary Bladder.—Saxer[13] described an intensely black fleck consisting of pigmented connective tissue resembling choroid, in a bladder teratoma. Schurch[59] noted the occurrence of pigment cells in clumps and circular structures spontaneously suggesting rudimentary optic cups.

Teratoma of the Kidney.—Lubarsch[60] reported a teratoma of the kidney in a female infant containing "choroid-like formations" of pigment epithelium in strands and lining cavities.

Brief reviews of optic anlages in teratomas and dermoids of the ovary appear in the works of Miller[61] and Selye.[62] The latter presents the only summary to be found in English.

COMMENT

Budde[63] criticized the interpretation of cysts lined with pigmented polygonal cells and pigmented connective tissue as optic anlages—specifically in the cases of Baumgarten, Kappeler, Kroemer and Katsurada, although acknowledging as justified the macroscopic optic rudiment of Klebs. Budde cited the normal occurrence of pigmented connective tissue in the meninges and the absence of the elements of retina in the aforementioned cases. He denied that a gross, thinned, transparent cyst was cornea and stated that pigmented cysts and canals represented modified ependyma.

53. Poult, J.: Ein Teratom der Thyreoidea, Virchows Arch. f. path. Anat. **181**:101, 1905.

54. Hunziker, H.: Die Teratome der Schilddrusengegend, Beitr. z. Geburtsh. u. Gynäk. **13**:448, 1909.

55. Ehlers, H.: Ueber ein Teratoma embryonale der Schilddrusengegend, Beitr. z. path. Anat. u.z. allg. Path. **57**:46, 1913-1914.

56. Russel, A. W., and Kennedy, A. M.: Teratoma of the Thyroid in a Fetus, J. Obst. & Gynaec. Brit. Emp. **23**:109, 1913.

57. Schönberg: Zur Lehre des Teratoms der Schilddruse, Inaug. Dissert., Basel, 1911; cited by C. Wegelin, in Lubarsch and Henke,[60] 1926, vol. 8, p. 312.

58. Footnote deleted.

59. Schurch, O.: Ueber ein Teratom der Harnblase, Ztschr. f. Path. **29**:173, 1923.

60. Lubarsch, O., and Henke, F.: Handbuch der speziellen pathologischen Anatomie und Histologie des Auge, Berlin, Julius Springer, 1925, vol. 6, pp. 700 and 702.

61. Miller, J.; cited by Lubarsch and Henke,[60] 1937, vol. 7, pt. 3, pp. 426 and 442.

62. Selye, H.: Encyclopedia of Endocrinology, Montreal, Richardson, Bond & Wright, 1946, sect. 4, vol. 7, p. 224.

63. Budde, M.: Ueber die Genese der Fetalinklusionen, Beitr. z. path. Anat. u.z. allg. Path. **75**:357, 1926.

Budde demanded that a structure to be considered an optic anlage must show a rudiment of the lens. There are, however, no clearcut instances of lens anlages to be found in the literature. Budde was the first to cite the importance for teratology of the experimental work of Spemann,[64] who transplanted optic anlage-determined tissues and obtained eyes with lenses. Heijl [28b] mentioned a Russian named Kordis who found lenses in a dermoid cyst. The figures of Magarinos Torres and associates [53] suggest lens fibers, but it would be easier to accept the validity of that interpretation in the presence of an associated optic cup.

It is curious that the occurrence of lenses in teratomas is so rare, especially in view of experimental evidence in amphibia (after removal of the lens from the eye of frogs and salamanders, a new lens can be regenerated from the neural ectoderm at the edge of the optic cup) suggesting that "the lens may be regarded as a secondary modification which can be produced promiscuously in response to the need of the optic cup" (Mann,[7] page 23). It may be that the absence of neighboring, undifferentiated surface ectoderm from which the lens plate normally develops is responsible.

The weight of evidence in my case and in others seems effectively to dispose of Budde's dictum.

In a study of the histogenesis of neural tissue, Willis [65] described neuroepithelial cysts without pigment resembling optic anlages. He noted a close relation between neuroepithelial and epidermal tissue. As a result of serial sections of many teratomas, he stated that there are multiple foci of a primitive, plastic epithelium which may differentiate into either neural or epidermal tissue, just as occurs in the embryo. He stressed the importance of "organizer" activity in the teratoma.

Willis [66] in a comprehensive discussion of teratomas, made the surprising statement that "there is no justification for speaking of 'eyes' in teratomas." Others (Willis,[66] Budde,[53] Corsy and associates [21] and Askanazy [24]) have suggested that many of the pigmented neuroepithelial masses, tubules and cysts are not necessarily optic anlages, a view given additional support by the studies in pigment formation establishing the neural crest origin of pigment cells (Dushane,[67] Masson [68]). But to deny that the teratomatous eye in the present case

64. Spemann, H.: Embryonic Induction and Development, Silliman Memorial Lecture, New Haven, Conn., Yale University Press, 1938.

65. Willis, R. A.: The Histogenesis of Neural Tissues in Teratomas, J. Path. & Bact. **42**:411, 1936.

66. Willis, R. A.: The Pathology of Tumors, St. Louis, C. V. Mosby Company, 1948, p. 959.

67. Dushane, G. P.: Development of Pigment Cells in Vertebrates, New York Acad. Sc. (spec. publ.) **4**:1, 1948.

68. Masson, P.: Pigment Cells in Man, New York Acad. Sc. (spec. publ.) **4**:15, 1948.

is an eye is to deny that a piece of teratomatous skin is skin, even though it corresponds in minute detail to that organ and would be so called by any pathologist. While it is curious that in the fetiform teratomas, in which one would expect a high degree of differentiation, the eyes are represented only by pigment spots; nevertheless, these spots occur just where eyes should occur and are exactly two in number.

CONCLUSION

The literature dealing with the formation of rudimentary eyes in teratomas is reviewed. The following facts emerge:

1. Rudimentary eyes produced by both benign and malignant teratomas, occurring anywhere in the body, are nearly always malformed and of limited development.

2. They may be of macroscopic size, as in dermoid cysts, or essentially microscopic, as in most solid teratomas.

3. They may occur singly, paired or in considerable numbers.

4. Their architecture varies from simple cysts lined partly or wholly with pigmented or nonpigmented neuroepithelium, which probably do not all represent the visual organ, to clearcut and undeniable optic cups.

5. The cups are composed of an outer, pigmented layer and an inner, nonpigmented layer of neuroepithelium, which may show early retinal differentiation, as in the present case.

6. Choroid and retina are frequently encountered; eyelids, cornea, vitreous and sclera, occasionally; the lens is rarely formed.

7. Malignant change has been reported in a number of teratomas showing the characteristic appearance of neuroepithelioma retinae. Widespread metastases may occur, which even reproduce the structure of the more undifferentiated optic anlages.

A case is presented of a malignant ovarian teratoma containing a well formed optic cup. Half the inner wall of the cup showed the approximately normal development of the 15 mm. (5 to 6 week) embryonic retina. The other half consisted of an undifferentiated tissue, closely resembling neuroepithelioma retinae.

340 East Fifty-Second Street.

ANEURYSM OF THE INTERNAL CAROTID ARTERY SIMULATING TUMOR

Report of a Case

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THE CASE to be reported illustrates the similarity of the clinical picture in aneurysm of the internal carotid artery and in basal neoplasm. Arteriography, in which roentgenograms are taken after the injection of iodopyracet U.S.P. (diodrast®) into the common carotid artery, provides an excellent means of portraying and localizing an aneurysm and might in this case have helped to establish the diagnosis before operation.

REPORT OF CASE

Mrs. P. S., aged 59, consulted me at my office on Sept. 9, 1947. She had been referred for a disorder of the lacrimal passages of the right eye, for which she had been treated by repeated probings, without result. I diagnosed this condition as an infection localized to the lacrimal canaliculus of the lower lid and cured it by slitting the duct with a Weber knife.

My attention was then directed to an obvious right convergent strabismus of paralytic type. The patient stated that diplopia had developed four years previously and that the right eye had subsequently turned inward. During the same period she had slowly lost most of the vision of that eye. She described a periodic "dull, heavy feeling" in the right eye and frontal region.

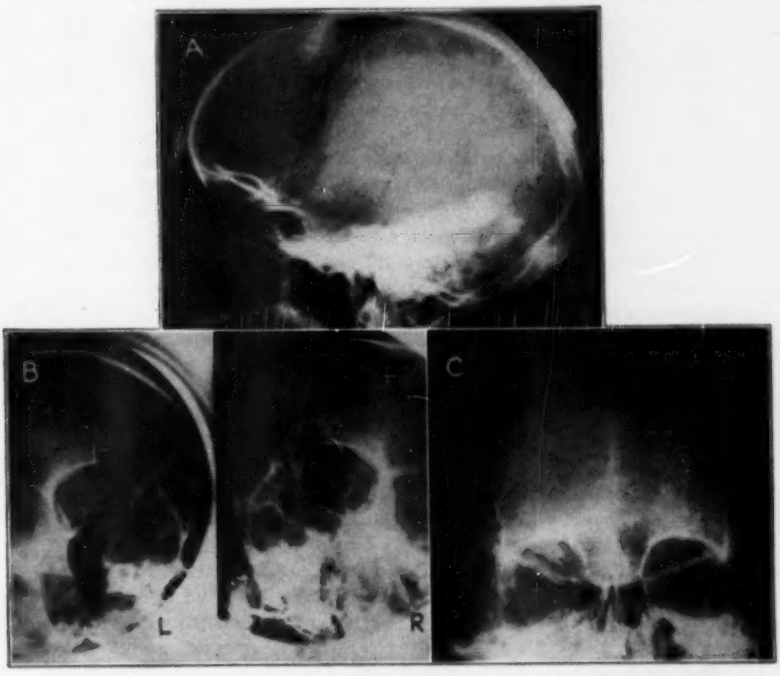
She was weak and at times became dizzy. She had not lost weight; her appetite was good. During the past eight years she had been under the constant care of an able internist for persistent vascular hypertension, the pressure ranging in the neighborhood of 240 systolic and 120 diastolic. The patient had been told that the ocular paralysis resulted from a "stroke."

On April 19, 1948 vision in the right eye was limited to counting fingers at 6 inches (15 cm.) in the nasal field; vision in the left eye was 16/200, with correction it was 20/25, and she could read Jaeger type 1. There was slight ptosis of the right eye. The right globe was markedly convergent, with excursions restricted in all directions of gaze. The right pupil was moderately dilated; it reacted faintly to direct light, but the consensual response was active. The right cornea showed definite hypesthesia. There was no exophthalmos or pulsation of the globe. The media appeared entirely clear. The optic nerve presented marked pallor, with clearly outlined margins; the retinal arterioles were highly sclerosed, and there was arteriovenous nicking of pronounced character.

The left eye was normal in all respects except for retinal arteriosclerosis. The optic nerve head appeared normal, and the field of vision was unrestricted.

Presented at the meeting of the New York Academy of Medicine, Section of Ophthalmology, May 16, 1949.

Roentgenographic examination of the skull (figure), by Dr. Henry Greenfield, was reported as follows: "The sella turcica is unusually large, and the dorsum sellae and the posterior clinoid processes are destroyed. The floor of the sella is involved, and the underlying sphenoid is slightly hazy. The left optic foramen is oval and well defined and reveals no irregularities in its outline. There is definite destruction of the inferior border of the right optic canal, with associated erosion of the adjacent outer border of the orbital plate. The inner aspect of the lesser wing of the right sphenoid bone is eroded. The findings are compatible with a tumor of the right sphenoid ridge or a primary lesion of the sella with secondary involvement of the sphenoid ridge"



A, lateral roentgenogram of the skull, showing large sella turcica and erosion of the dorsum sellae and posterior clinoid processes; *B*, roentgenograms showing normal left optic foramen and erosion of the right optic foramen; *C*, antero-posterior roentgenogram of the skull, showing erosion of the right sphenoid ridge.

In May 1948 the patient was hospitalized at Beth Israel Hospital, where the findings aforenoted were corroborated. A general medical survey, including neurologic examination, did not yield any additional facts. The preoperative diagnosis was meningioma of the right sphenoid ridge.

Through a craniotomy in the right frontotemporal region the middle cranial fossa was explored, exposing a very large, pulsating aneurysmal mass. The flaps were replaced, and the wound was sutured. An incision was made along the

anterior border of the right sternocleidomastoid muscle, extending from the angle of the jaw to the thyroid cartilage. The common carotid artery was ligated slowly with a heavy silk suture. After waiting ten minutes, during which time the patient exhibited no signs of impairment of cerebral circulation, the right external carotid artery was ligated. The wound was closed.

Convalescence was rapid. After operation, the patient had extensive ecchymosis of the lids and face, complete ptosis of the upper lid of the right eye and an immobile, slightly proptosed right globe. After a few weeks the ecchymosis cleared entirely. After several months the upper lid returned to an almost normal position, and the globe has since receded and recovered some motility. The patient has continued to have some headache and pain.

A woman aged 59 had periodic pain in the right eye and frontal region of four years' duration. She had generalized arteriosclerosis and an extremely high blood pressure of many years' standing. Ocular examination revealed ophthalmoplegia and primary optic nerve atrophy of the right eye and hypesthesia of the right cornea. Roentgenograms of the skull showed erosion of the right optic canal and adjacent border of the orbital plate, erosion of the right sphenoid ridge and destruction of the dorsum sellae and posterior clinoid process. The preoperative diagnosis was meningioma of the right sphenoid ridge. On operation, a large aneurysm, probably arteriosclerotic in origin, of the intracranial portion of the internal carotid artery was exposed. The common and external carotid arteries were ligated in the neck.

COMMENT

Aneurysm of the internal carotid artery before rupture produces a syndrome that greatly resembles that of neoplasm at the base of the skull. Given a case of unilateral ophthalmoplegia,[1] with or without involvement of the optic pathways, clues to the site of a basal lesion, aneurysm or neoplasm or other abnormality, are as follows: diminution or absence of corneal sensation; moderate, rather than maximal, dilatation of the pupil with an abolished or sluggish direct light reflex, and anomalous movements of the lid and pupil, such as the pseudo-Graefe sign and the pseudo Argyll Robertson pupil.[2] Severe ocular pain and frontal headache in the presence of paralysis of the third nerve should direct suspicion to the possibility of an aneurysm of the internal carotid artery. The final diagnosis must rest on the results of roentgenologic and arteriographic findings. The importance of early diagnosis must be stressed, for hemorrhage from a leaking aneurysm is often ultimately fatal.

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1. Levitt, J. M.: Unilateral Ophthalmoplegia Totalis: Parasellar Osteochondroma, Arch. Ophth. **12**:877 (Dec.) 1934.

2. Walsh, F. B., and King, A. B.: Ocular Signs of Intracranial Saccular Aneurysms: Experimental Work on Collateral Circulation Through the Ophthalmic Artery, Arch. Ophth. **27**:1 (Jan.) 1942.

CORNEAL FISTULA FOLLOWING TRANSPLANTATION

Report of Two Cases; Methods of Treatment

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WITH an increase in the number of corneal transplantations performed, there is also an increase in the various types of complications that occur. Much emphasis is placed on improvements in technic of the operation, and great advances have been made along this line; but together with this there must be improvement in the methods and technics of remedying the various complications, of which there are many.

Surgeons doing corneal transplantation are occasionally faced with the undesirable development of a corneal fistula, and it is the purpose of this paper to discuss briefly this complication and to deal with the methods of closure.

After the corneal transplantation, on careful observation of the wound and with the use of fluorescein, one may find a variable degree of seepage of aqueous along a border of the graft, even though the graft may appear to fit well in the cornea of the host and the anterior chamber be quite well formed. Theoretically, the area of cornea supplied in grafting should correspond to that removed from the host, but physiologically the wound usually allows aqueous to escape for the first twenty-four to forty-eight hours, until either the tissue edema that follows transplantation blocks the wound more securely or the epithelial regeneration covers the edges of the wound. Infiltration and fibrosis begin along the edge of the graft with the implantation, and this process is well advanced by seven to ten days, at which time the sutures are usually removed.

However, the normal process of epithelization and fibrosis of the borders of graft and host cornea may not follow, owing to improper apposition of the graft or to possible failure in viability of the graft at an isolated spot, with the resultant development of a fistula. In such circumstances, the corneal epithelium in its regeneration follows the edge of the host cornea over its border downward toward the anterior chamber covering the substantia propria in the same manner as that in

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which epithelium may enter the anterior chamber by following the wound after cataract extraction. When this occurs, a fistula forms at the site and a persistent flow of aqueous results. This may be slight, and even insufficient to allow the anterior chamber to collapse, or it may be large enough for the outflow to equal the reformation of aqueous, in which case the anterior chamber remains completely collapsed. This picture will at one time or another be presented to the surgeon who does corneal transplantation, and the proper handling of this complication may mean the success or failure of a previously well performed grafting operation. The corneal fistula must be closed promptly and securely, as failure to do so renders the eye susceptible to the development of glaucoma and the formation of anterior synechia.

METHODS OF CLOSURE

Corneal fistula can be closed by employing either of the following methods: (1) the usual means of cauterization, either thermal or

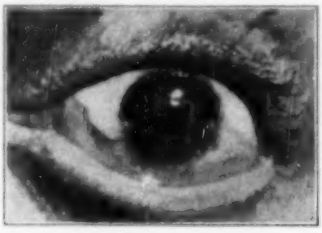

Fig. 1.—Clear square corneal transplant with minute fistula at one corner of graft. Closure was completed with cauterization.

chemical, or (2) the method advocated and introduced by me, which consists in transplantation of a mucous membrane graft to a previously curetted fistulous tract.

The various methods of cauterization with chemicals, such as iodine or trichloroacetic acid, or the application of the thermal cautery are advocated for destroying the epithelial lining of the small, more minute fistulas, and in cases of such defects these methods are often sufficient to promote fibrosis and seal the opening. Such a problem was encountered in the case shown in figure 1. Along the temporal border of this graft a fistula developed. It was very small, and the aqueous did not escape in sufficient quantity to allow the anterior chamber to collapse. This tract was cauterized on two occasions with 2 per cent iodine and remained thereafter closed securely. No opacification, vascularization or increase in intraocular pressure followed, and the graft continued to be perfectly transparent.

If the simple methods of cauterization fail to close the fistula, the other method, that of suture and conjunctival transplantation, may be carried out. Suture of a corneal fistula without the use of transplant tissue to bridge the gap is impractical, because there is no laxity in the tissue when one attempts to draw the borders together. Consequently, in cases of the larger fistulas closure is brought about by bridging the tract with a small piece of mucous membrane and securing this firmly

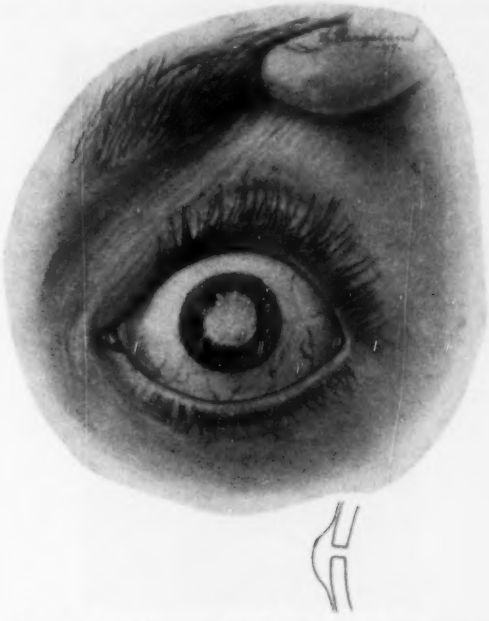

Fig. 2.—Drawing of large corneal fistula at border of opaque graft.

with a suture placed directly through the opposite walls of the fistula. Figure 2 is a drawing of a corneal transplant which became completely opaque six weeks after operation, and several weeks later a fistula was observed to be present. Figure 3 shows a magnified photograph of the fistula. The corneal epithelium was grown over this fistula in bleb formation, but not securely, and the aqueous leaked from the edge of the bleb. Removal of the bleb revealed a smoothly lined sinus tract extending through the cornea into the anterior chamber. In an attempt to close this fistula, repeated curettages were made to remove the

epithelial covering and to cauterize the tract. These procedures were of no avail, and the sinus continued to drain aqueous.

The following procedure was then carried out. The corneal epithelium was removed from the region of the tract, and the sinus was thoroughly curetted and cauterized with iodine. A 000000 atraumatic silk suture was then passed through the apposing walls of the sinus directly through the middle of the tract. A small piece of bulbar conjunctiva was then removed and placed over and into the sinus tract and the suture tied securely over the mucous membrane graft. This

Fig. 3.—Photograph of corneal fistula illustrated in figure 2, showing draining bleb.

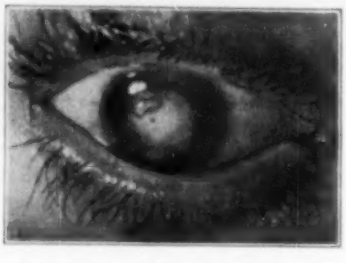

Fig. 4.—Postoperative mucous membrane graft in place in fistulous tract after removal of suture.

suture was allowed to remain in place for two weeks, after which time it was removed. Figure 4 shows the mucous membrane graft in place after the suture had been removed. It appears somewhat raised from the surrounding cornea, but it is securely in place. In figure 5, *a* illustrates the technic employed and shows the silk suture through the apposing walls of the sinus tract; *b* shows the mucous membrane graft in place, and *c* the suture tied over the mucous membrane graft.

Three weeks after operation there appeared a slight degree of vascularization extending downward from the corneal limbus to the

mucous membrane graft. This was treated, and the vessels were destroyed by the application of 650 rep of beta radiation twice at a seven day interval.

The mucous membrane graft became covered with corneal epithelium and completely adherent to the fistulous area, which it sealed. The anterior chamber was restored and remained formed, and repeated obser-

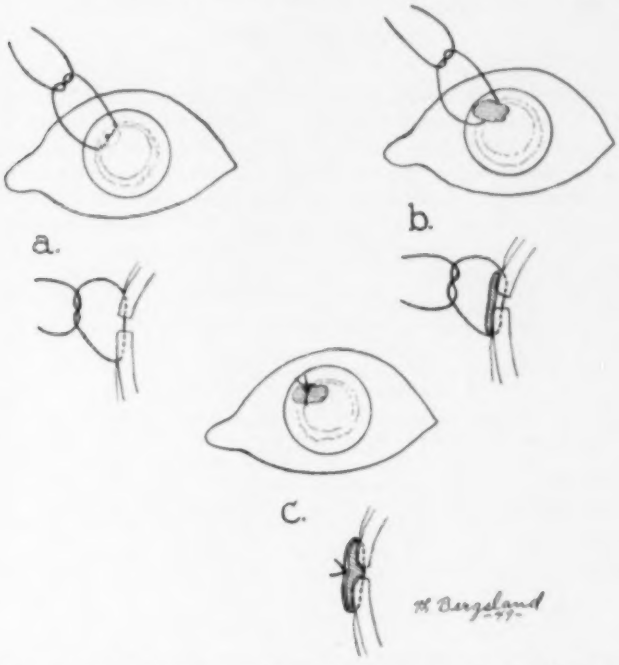

Fig. 5.—(*a*) Silk suture placed through apposing walls of corneal fistula; (*b*) mucous membrane graft in place over fistulous tract; (*c*) mucous membrane graft and suture tied securely.

vations with the slit lamp and with the aid of fluorescein staining failed to reveal any outflow of aqueous. Gradual shrinkage of the mucous membrane graft took place. This graft no doubt acted as a scaffold for fibrosis and then became gradually replaced by the usual corneal fibrosis, for after six months it was difficult to ascertain the location of the mucous membrane graft.

SUMMARY

1. A corneal fistula may develop after corneal transplantation.

2. Closure of this fistula may be obtained either by cauterization or by the transplantation of mucous membrane into the fistulous tract.

3. The mucous membrane graft gradually becomes a part of the scar tissue which it supports.

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EPITHELIAL INVASION OF ANTERIOR CHAMBER FOLLOWING CATARACT EXTRACTION

Effect of Radiation Therapy

MORRIS H. PINCUS, M.D.
BROOKLYN

EPITHELIAL invasion of the anterior chamber is a most malignant postoperative complication of cataract extraction. Estimates of the incidence vary from 0.06[1] to 0.11 per cent.[2] When one considers the number of cataract extractions that are performed by surgeons of varying abilities and with various methods, the incidence of this complication is remarkably low. Since this is an infrequent complication, the finding of 5 cases during the past two years merits report.

REPORT OF CASES

CASE 1.—Mr. P. J., aged 70, was examined at the Kings County Hospital. A mature cataract in the right eye and an immature cataract in the left eye were noted on routine ophthalmologic examination. The preoperative physical and laboratory studies[3] revealed little of clinical significance.

A preliminary iridectomy of the right eye was performed on Aug. 20, 1947. The patient was readmitted to the hospital for extraction of the cataract on September 29. The operative notes follow.

"The usual preparation of the eyelids was carried out. Anesthesia with epinephrine hydrochloride, butacaine sulfate (butyn®) and cocaine was produced with the drop method. The cul-de-sac was irrigated thoroughly. A 0000 black silk suture was passed through the superior rectus muscle. An incision was made in the corneal limbus from 11 to 1 o'clock with the keratome and the section enlarged

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Read before the Brooklyn Ophthalmological Society, April 21, 1949.

From the Department of Ophthalmology, Long Island College Hospital and College of Medicine; Mortimer A. Lasky, M.D., Ophthalmologist in Chief (Acting).

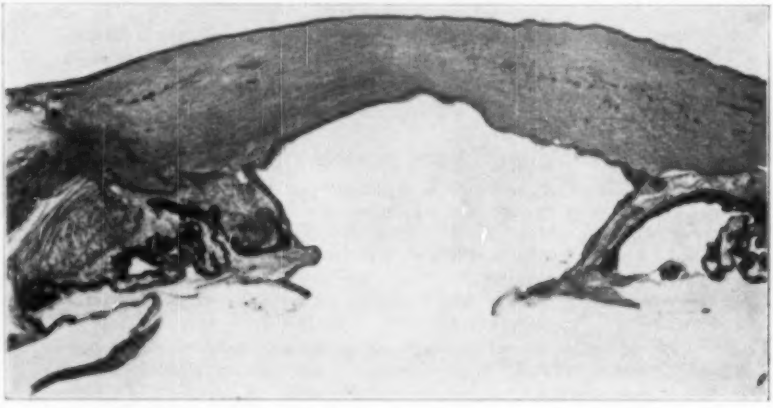
1. Terry, T. L.; Chisholm, J. F., and Schonberg, A. L.: Studies on Surface Epithelium Invasion of the Anterior Segment of the Eye, Am. J. Ophth. **22**:1083, 1939.

2. Theobald, G., and Haas, J.: Epithelial Invasion of the Anterior Chamber Following Cataract Extraction, Tr. Am. Acad. Ophth. **53**:470, 1948.

3. The blood pressure was 140 systolic and 70 diastolic. The Wassermann reaction of the blood was negative. Urinalysis showed specific gravity of 1.021 and amber, clear fluid, with no sugar or albumin. The patient was edentulous. The nasolacrimal sacs were patent. Cultures of material from the conjunctiva yielded occasional diphtheroids in the right eye and occasional Staphylococcus aureus in the left eye. Tension was 23 mm. (Schiøtz) in the right eye and 28 mm. in the left eye.

with Stevens scissors. Attempts to grasp the capsule of the lens were ineffectual. The lens capsule was opened with the cystotome, and, by means of traction and countertraction, the lens was extracted. The lens capsule was removed with the Kalt forceps. Corneoscleral sutures, previously placed at 1, 12 and 11 o'clock, were tied. The iris pillars were reposited. The suture in the superior rectus muscle was removed. Drops of atropine and mercury bichloride ointment were instilled. A dressing for both eyes and a mask were applied."

Four days after operation the cornea was cloudy. There was a small amount of blood in the anterior chamber and striate keratitis was present. The anterior chamber was shallow. The eye was red and painful. The patient was given an injection of foreign protein (milk). Five days later, the eye was unchanged in appearance, and he was given foreign protein (typhoid and paratyphoid vaccine) intravenously. The patient was discharged on the seventeenth postoperative day with a congested globe, semiclouded cornea and shallow chamber.



Epithelization of the anterior chamber following cataract extraction.

Six weeks later the pericorneal congestion was still intense and the cornea very hazy. Examination with the slit lamp revealed a brushlike vascularization at the limbus, the blood vessels penetrating the corneal stroma 1 to 2 mm. The anterior chamber appeared shallow. There was a fine grayish sheen on the posterior surface of the cornea, and a diagnosis of epithelial downgrowth was made. Radiation therapy [4] was instituted.

Two months later the grayish sheen on the posterior surface of the cornea was unchanged. The eye was soft and painful. The fundus could not be visualized.

4. Dec. 2, 1947: Radium radiation was administered with the following technical factors: radon plaque, 1.5 by 1.5 cm., with filtration through glass; 14 millicuries; time, three minutes; total dose, 42 millicurie minutes. Dec. 9 to 23, 1947: Roentgen radiation was delivered, with the following technical factors: 100 kilovolts; 5 milliamperes; 200 r; 15 cm. from the eye; no additional filtration; total dose 2,000 r.

There was no vision in the eye. Enucleation was performed on Feb. 2, 1948, four months after the cataract extraction.

Pathologic Report (figure).—The cornea was thickened throughout. At the limbal ends there was much interstitial vascularity. At one place in the corneoscleral junction there was a through and through wound with rupture and wrinkling of the posterior elastic membrane (Descemet's membrane). The edges of the wound were poorly apposed. Anterior synechias were present, leaving a very shallow anterior chamber. Laminated corneal epithelium lined the entire posterior surface of the cornea, continued over the angle of the chamber and covered the entire exposed anterior surface of the iris and part of the anterior hyaloid membrane. The uveal tract was edematous, and opposite the operative wound the choroid was detached by an organized hemorrhage. The retina was completely detached and was atrophic. The posterior segment, containing the optic nerve, was missing from these sections.

The diagnosis was epithelial invasion of the anterior chamber following cataract extraction; subchoroidal hemorrhage with choroidal detachment, and retinal detachment with subsequent atrophy.

Case 2.—Mr. F. T., aged 74, was examined at the Brooklyn Eye and Ear Hospital on Jan. 17, 1948. Routine ophthalmologic examination revealed maturing cataracts. Vision was 20/200 in the right eye and 20/70 in the left eye. Except for the finding of hypertension, the routine preoperative physical and laboratory studies [5] were of little clinical significance.

On April 20, 1948 the right lens was extracted. The operative note for akinesia follows: "With the O'Brien method of infiltration and a retrobulbar injection of procaine hydrochloride with local instillations of tetracaine, the right eye was routinely prepared. A corneoscleral incision was made with the keratome and the section was enlarged with the Stevens scissors. Three 00000 black silk corneoscleral sutures were placed at 2, 12 and 10 o'clock, in readiness to tie. The iridectomy was performed. After several unsuccessful attempts with the Verhoeff capsule forceps, the Dimitry suction cup was applied. A large intumescent lens was removed. The sutures were tied. The iris pillars were reposited. Atropine and nitromersol N. F. (metaphen®) drops were instilled. Eye pads and a mask were applied."

On the second postoperative day hyphema and striate keratitis were noted. On the fourth day the patient complained of pain in the eye, and blood was found on the dressing. The bleeding subsided spontaneously. There was no fundus reflex. On the tenth postoperative day a slight fundus glow was visible inferiorly. The anterior chamber was shallow. The eye was congested.

Approximately six weeks later the cornea was still hazy. Examination with the slit lamp revealed a grayish sheen on the posterior surface of the upper half of the cornea. The anterior chamber was very shallow. The fundus could not be visualized. Vision was limited to the perception and projection of light.

A diagnosis of epithelial invasion of the anterior chamber was made, and the patient was referred to the Long Island College Hospital for roentgen therapy.

5. The blood pressure was 196 systolic and 112 diastolic. The Wassermann reaction was negative. The urine contained no sugar or albumin. The nasolacrimal sacs were patent. Smears of conjunctival secretions showed no pathogens. Examinations of the teeth, ears, nose and throat did not reveal any foci of infection.

The patient received a series of five roentgen treatments.[6] When he was last examined, on March 31, 1949, there was distinct improvement. Examination with the slit lamp revealed clearing of the grayish sheen on the posterior surface of the cornea to within 2 mm. of the upper limbus. In the region of the interpalpebral fissure, there was, however, an area of turbidity just below the anterior surface of the cornea, which possibly was the beginning of band keratitis.

The vitreous was full of free-floating opacities. The fundus could not be visualized. Vision had increased, and the patient was able to count fingers at 2 feet (60 cm.). Tension (Schiøtz) was 48 mm. of mercury in the right eye and 20 mm. in the left eye. The patient had no pain. There was no congestion of the globe.

CASE 3.—Mr. V. G., aged 75, was examined at the Brooklyn Eye and Ear Hospital on Jan. 30, 1946. Routine examination of the eyes revealed mature cataracts. Vision was limited to counting fingers at 3 feet (90 cm.) in the right eye and was 20/200 in the left eye.

The preoperative physical and laboratory examinations[7] revealed generalized arteriosclerosis with mild hypertension.

On Sept. 10, 1946 the right lens was extracted. The operative note read as follows: "Retrobulbar and modified Van Lint infiltrations with procaine, as well as topical instillations of tetracaine, were made for akinesia and anesthesia. A suture was placed in the superior rectus. The corneoscleral section, with a superior conjunctival flap, was made with the Graefe knife. Iridectomy was performed. The lens was extracted extracapsularly. The conjunctival sutures were tied; the iris pillars were reposited, and an air bubble was instilled. Atropine and nitromersol drops were instilled. Eye pads and a mask were applied. The patient left the operating room in good condition."

Recovery was uneventful. The patient was discharged from the hospital on the tenth postoperative day.

A discission was performed on June 18, 1947, and the patient was discharged three days later with a good pupillary opening. With a correction of + 11.00 D. sph. ⊂ + 2.00 cyl., axis 175, vision in the right eye was improved to 20/40.

The lens of the left eye was extracted on May 3, 1948. The operative notes read as follows: "After O'Brien and retrobulbar infiltrations with procaine, as well as local instillations of tetracaine, a corneoscleral section was made with the keratome and enlarged with the Stevens scissors. Three black silk corneoscleral sutures were placed in readiness to tie at the 10, 12 and 2 o'clock positions. After the iridectomy, the lens was delivered in capsule with the Verhoeff capsule forceps. The sutures were tied. The iris pillars were reposited. Atropine and nitromersol drops were instilled, and eye pads and a mask were applied."

On the second postoperative day the cornea was hazy. The anterior chamber appeared to be reforming. On the fourth postoperative day the patient complained of pain in the eye. The globe was congested. There was no fundus reflex. On the

6. The technical factors were as follows: cone port, 2 cm.; filtration, 2 mm. of aluminum; 125 kilovolts; 5 milliamperes; 300 r; distance from the eye, 35 cm.; time, eleven minutes fifteen seconds; total dose, 1,500 r.

7. The Wassermann reaction of the blood was negative. The urine contained no sugar or albumin. The blood pressure was 160 systolic and 80 diastolic. Examination of the teeth, ears, nose and throat revealed no foci of infection. Tension (Schiøtz) was 20 mm. of mercury in each eye. The nasolacrimal sacs and ducts were patent on irrigation. Conjunctival smears showed epithelial cells but no organisms.

eighth day the anterior chamber was filled with blood. The patient was discharged on the sixteenth postoperative day with wrinkling of the posterior elastic membrane, a shallow anterior chamber, marked vitreous haze and a very dull fundus reflex.

One month later the eye was still congested. On examination with the slit lamp, a grayish, filmy sheen was visible on the upper half of the posterior surface of the cornea, as well as on the anterior surface of the nasal pillar of the iris. The fundus could not be seen. There was no fundus reflex. The eye was soft to palpation. A diagnosis of complete retinal detachment and epithelial invasion of the anterior chamber was made. The patient was referred to the Long Island College Hospital for roentgen therapy.

A series of nine roentgen treatments[8] was given the patient. The corneal haze remained, and the grayish sheen on the posterior surface of the upper half of the cornea and on the anterior surface of the nasal iris pillar, though apparently thinner, seems only to have been checked in its downward progression. Vision in the right eye, with correction, remained 20/40. There was no vision in the left eye. Tension (Schiøtz) was 21 mm. of mercury in the right eye and 18 mm. in the left eye.

Case 4.—Mr. T. J. N., aged 74, was examined at the Brooklyn Eye and Ear Hospital on April 7, 1947. Ophthalmologic examination revealed a mature cataract in each eye. Vision was limited to 2/200 in each eye. The preoperative physical and laboratory examinations[9] disclosed little of significance except for generalized arteriosclerosis with mild heart failure.

The right lens was removed on June 28, 1947. The operative notes read as follows: "A modified Van Lint infiltration, as well as an O'Brien and a retrobulbar injection of procaine, was made. Tetracaine and epinephrine drops were instilled locally. A bridle suture was placed in the superior rectus muscle. The Graefe section made from 10 to 2 o'clock, was enlarged with the Stevens scissors. Corneoscleral sutures were placed at 10, 12 and 2 o'clock. Iridectomy was performed. The lens was removed in capsule with the Dimitry suction instrument. The sutures were tied, and the iris pillars were reposited. An air bubble was used to fill the anterior chamber. Atropine and nitromersol drops were instilled. Eye pads and a mask were applied."

Recovery was uneventful. On August 23 vision in the right eye was 20/50 with a correction of + 11.00 sph. ⊂ + 1.00 cyl., axis 180.

On Nov. 18, 1947 the patient returned with a red and painful right eye. Examination with the slit lamp revealed a fine, silky gray sheen covering the upper two fifths of the posterior surface of the cornea. Tension of the eye was felt to be elevated on digital examination. A diagnosis of epithelial invasion of the anterior chamber was made, and the patient was referred to the Long Island College Hospital for roentgen therapy.

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8. The technical factors were as follows: cone port, 2 cm.; filtration, 2 mm. of aluminum; 125 kilovolts; 5 milliamperes; 300 r; distance from the eye, 35 cm.; time, eleven minutes fifteen seconds; total dose, 2,700 r.

9. The Kahn reaction of the blood was negative. The urine contained no sugar or albumin. The blood pressure was 130 systolic and 90 diastolic. Examination of the teeth, ears, nose and throat revealed no foci of infection. The nasolacrimal sacs and ducts were apparently patent on irrigation. Tension (Schiøtz) in each eye was 24 mm. of mercury.

On Dec. 18, 1947, the gray silky sheen on the posterior surface of the cornea appeared to be somewhat thinner, and there apparently was no progression downward. Vision, with correction, remained at 20/40.

On April 15, 1948 vision in the right eye was reduced to 20/100. The downgrowth on the posterior surface of the cornea appeared to be unchanged. The eye was white and nontender. The fundus could not be visualized. The vitreous appeared to be filled with blood.

On May 27 vision in the right eye was reduced to perception of light.

The left lens was removed on Oct. 26, 1948. The operative notes read as follows: "The usual preoperative injections and local instillations were made. A 3 mm. conjunctival flap was formed circumcorneally, from 3 to 9 o'clock. Modified Stallard corneoepiscleroconjunctival sutures were inserted at 10 and 2 o'clock. The keratome incision was made at 12 o'clock, and the section was enlarged with Stevens scissors to 3 and 9 o'clock subconjunctivally. The lens was extracted in capsule with the Verhoeff capsule forceps. The sutures were tied. The iris pillars were reposited. The conjunctival flap was closed with a continuous black 000000 suture. Atropine and metaphen[9] drops were instilled, and a binocular dressing and mask were applied."

Recovery was uneventful. On December 14 vision in the left eye was corrected to 20/30 with a + 11.00 sphere. Vision in the right eye was still limited to perception of light.

On Feb. 16, 1949 vision in the right eye had returned to 20/40 with the original correction. The hemorrhage in the vitreous had been absorbed. The fundus was visible, and, except for a moderate degree of sclerosis of the retinal arteries, all structures appeared to be normal. The grayish sheen on the posterior surface of the cornea remained unchanged.

Between Nov. 18, 1947 and Feb. 16, 1949 the right eye had had five roentgen treatments.[10]

CASE 5.—Mr. J. P., aged 76, was examined at the Brooklyn Eye and Ear Hospital on Nov. 20, 1948. A mature cataract was noted in the right eye and an immature senile cataract in the left eye. Vision in the right eye was limited to light perception and light projection. Vision in the left eye was 20/200, correctible to 20/50 — 2.

The routine preoperative laboratory examinations[11] gave essentially normal findings. Physical examination revealed generalized arteriosclerosis with hypertension.

On Dec. 14, 1948 the right lens was extracted. The operative notes read as follows: "A traction suture was inserted in the superior rectus after akinesia and local anesthesia. A conjunctival flap was fashioned superiorly. Modified Stallard sutures were placed at 11 and 1 o'clock. A keratome incision was made at 12 o'clock, and the section was enlarged with Stevens scissors to 9 and 3 o'clock. After the iridectomy, the lens was removed in capsule with the Verhoeff capsule forceps. All sutures were tied, and the iris pillars were reposited. Atropine and nitromersol drops were instilled. Eye pads and a mask were applied."

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10. The technical factors were as follows: cone port, 2 cm.; filtration, 2 mm. of aluminum; 125 kilovolts; 5 milliamperes; 300 r; distance from the eye, 35 cm.; time, eleven minutes fifteen seconds; total dose, 1,500 r.

11. The Kahn reaction of the blood was negative. The urine contained no sugar or albumin. Examinations of the teeth, ears, nose and throat revealed no foci of infection. The nasolacrimal sacs and ducts appeared patent on irrigation. The blood pressure was 180 systolic and 80 diastolic.

On the second postoperative day there was moderate striate keratitis. The anterior chamber was reforming and clear.

On the fourth postoperative day, the patient complained of pain in his eye, and it was noted that the anterior chamber was filled with blood. The patient was discharged on the tenth postoperative day. The hemorrhage in the anterior chamber had almost completely absorbed. There was a good fundus reflex, but no details were visible.

On Jan. 4, 1949 the eye was still congested. The wound edges from 12 to 2 o'clock did not appear to be healing well, although the anterior chamber was reformed and intact. Examination of this area with the slit lamp revealed it to be covered by epithelium, but immediately below this area, and on the posterior surface of the cornea, there was a small rim of grayish tissue, no wider than 2 mm. There were a number of folds in the posterior elastic (Descemet's) membrane. No details of the fundus were visible at that time.

With + 12.00 sph. ⌒ + 2.00 cyl., axis 180 vision in the right eye was correctible to 20/50 on March 22. The fundus was dimly visible. The small rim of grayish tissue on the posterior surface of the cornea did not appear to have increased in size. Tension (Schiøtz) was 20 mm. of mercury in the right eye and 18 mm. in the left eye.

On April 19 the filmy gray tissue on the posterior surface of the cornea had advanced uniformly downward. A diagnosis of epithelial invasion of the anterior chamber was made, and the patient was referred to the Long Island College Hospital for radiation therapy.

COMMENT

Collins and Cross[12] (1892) were the first to describe the pathologic picture of epithelial invasion of the anterior chamber following a cataract extraction. In their patient glaucoma developed eight months after removal of the cataract, and the eye was removed two years later. Laminated epithelium covered the back of the cornea, the anterior surface of the iris, the capsule of the lens and the hyaloid membrane.

Meller,[13] in 1901, advanced the theory that the epithelial invasion of the anterior chamber was the result of proliferation of the epithelium along the surgical wound.

Collins,[14] in 1914, and Levine,[15] in 1933, pointed out that after the corneal section a fibrinous coagulum is rapidly formed between the two stromal surfaces of the incised cornea, but that the anterior and posterior edges of the wound remain agape. The corneal epithelium grows down into the wound proper until it is met by this fibrinous coagulum, in

12. Collins, E. T., and Cross, F. R.: Two Cases of Epithelial Implantation Cyst in the Anterior Chamber After Extraction of Cataract, Tr. Ophth. Soc. U. Kingdom **12**:125, 1892.

13. Meller, J.: Ueber Epitheleinsenkung und Cystenbildung im Auge, Arch. f. Ophth. **52**:436, 1901.

14. Collins, E. T.: Discussions on Post-Operative Complications of Cataract Extraction, Tr. Ophth. Soc. U. Kingdom **34**:18, 1914.

15. Levine, J.: Growth of Corneal Epithelium into the Anterior Chamber, Am. J. Ophth. **16**:796, 1933.

which fibrous tissue grows to connect the two stromal surfaces. As this fibrous tissue pushes forward, it gradually flattens the ingrowing epithelial plug, and a smooth layer of corneal epithelium finally covers the wound. Posteriorly, the fibrous tissue grows down to the endothelial layer of cells. If the original coaptation of the lips of the wound is not firm, the corneal epithelium, instead of being stopped by the fibrous plug of tissue, continues to grow straight through the wound into the anterior chamber. Here it lines the posterior surface of the cornea, the filtration angle and the anterior surface of the iris, thus forming a cyst of the anterior chamber.

Perera,[16] in 1937, stated that epithelium in the anterior chamber might manifest itself in three forms, namely, (1) pearl tumors of the iris, (2) post-traumatic cysts of the iris and (3) epithelization of the anterior chamber.

Terry and associates [1] in 1939, noted three ways in which epithelium could be introduced into the eye: (1) by implantation (ragged foreign body or instrument), (2) by a flap of conjunctival or corneal tissue turned into the eye and (3) by ingrowth of epithelium proliferating along the edges of a gaping wound or prolapsed tissue, or possibly along a corneal suture.

Corrado [17] attempted to explain by experiments on animals how epithelium invaded the anterior chamber. He found that it was not sufficient that a strip of epithelial tissue should fall into the anterior chamber for attachment and proliferation to occur. He showed that only when the corneal wound remained open was it possible for corneal epithelium, by proliferation, to penetrate into the anterior chamber after having covered the border of the wound itself. Causes which facilitated this development were the incarceration of the iris, the capsule of the lens and the vitreous in the corneal wound. The smoother the surface of implantation, the more easily did the epithelium tend to proliferate along that surface.

These experiments supported the clinical fact that epithelization of the anterior chamber occurs, as in the majority of cases reported, when there has been slow healing of the corneal wound, with delayed formation of the anterior chamber.

In order to make the clinical diagnosis of a lining of the anterior chamber by epithelial cells, one must first have this condition in mind. A slowly healing wound, delayed formation of the anterior chamber or

16. Perera, C. A.: Epithelium in the Anterior Chamber of the Eye After Operation and Injury, Tr. Am. Acad. Ophth. **42**:142, 1937.

17. Corrado, M.: Glaucoma secondario: A penetrazione e proliferazione di epitelio in C. A. in occhio operato di cataratta, Ann. di ottal e clin. ocul. **59**:706, 1931.

leaking aqueous are potential precursors. If, in addition, one discovers a thin haze on the posterior surface of the cornea, beginning at the wound and extending downward as time goes on, the possibility is no longer remote.[18]

A proliferating capsular remnant, especially when entangled in the wound, might, conceivably, simulate epithelium, but repeated examinations should disclose its true nature. Striate keratitis should offer no difficulty.

In the cases presented, the following complications occurred: in case 1, hyphema, a shallow anterior chamber, choroidal and retinal detachment; in case 2, massive intraocular hemorrhage, shallow anterior chamber; in case 3, massive intraocular hemorrage, shallow anterior chamber, complete retinal detachment; in case 4, late intraocular hemorrhage; in case 5 intraocular hemorrhage, poor healing of wound edges.

The time interval in which the epithelization of the anterior chamber was first clinically recognized varied from three weeks (case 5), to five months (case 4). Meller [18] reported the appearance of this complication in 1 case as early as four days after operation.

Epithelization of the anterior chamber, if allowed to progress, eventually destroys the eye through severe iridocyclitis and glaucoma. Any measure, therefore, which offers the slightest chance of arresting or retarding the development of this complication must be seriously considered.

Operative intervention is of no avail; if anything, it hastens the destruction of the eye. Cauterization, with the actual cautery, of the margin of the freshly made wound and the inner surface of the upper part of the cornea was first done by Fazakas. He claimed that there was no recurrence of the epithelial growth and attributed the success of this treatment to the irradiation with thermal energy.[18] Attempts to destroy or inhibit the epithelization of the anterior chamber by the use of roentgen rays or radium have been encouraging.

Vail [18] used the radium plaque [19] in 1 case and reported a complete cure in one and one-half years. Perera [16] used roentgen radiation in

18. Vail, D.: Epithelial Downgrowth into the Anterior Chamber Following Cataract Extraction: Arrest by Radium Treatment, Arch. Ophth. **15**:270 (Feb.) 1936.

19. A radium plaque 5/8 inch (15 mm.) square, containing 15 mg. of radium and covered with a very thin monel® metal protective screen with further filtration through two thicknesses of rubber stock, a total of about 1 mm. of rubber, was applied directly to the eyelid over the area involved and left on for two hours.

1 case. Two series of treatments [20] were given, and the growth completely disappeared. There was no evidence of its presence two years later. Theobald [2] stated that the use of roentgen rays in 3 cases were "without objective or subjective benefit."

Treatments were given in only 4 of the present series of cases. In case 1 both a radon plaque and a series of ten roentgen treatments were used, without improvement. The eye was enucleated. In case 2 a series of five roentgen treatments were given, with definite improvement. The epithelial downgrowth receded. In case 3 nine roentgen treatments were given. The downward extension of the epithelization of the anterior chamber appeared to have been arrested, as there was no progression of the growth after the institution of this therapy. In case 4 five roentgen treatments were received, and the appearance of the growth remained unchanged. Here, too, there was no further extension of the epithelial downgrowth after the institution of roentgen therapy. In case 5, at the time this report was written, no radiation therapy had been given.

In this small group of cases the use of roentgen therapy was definitely beneficial. The epithelial downgrowth was arrested in 2 cases, but it did not disappear or decrease in size with the therapy. In 1 case the growth definitely receded, but a corneal dystrophy (band keratitis) developed. No beneficial effects were noted in case 1, and the eye was eventually enucleated.

Prevention, rather than treatment, should be our aim. Collins,[14] in 1914, stated "that if a conjunctival flap is made to cover the corneal wound, a plug of epithelium does not grow into the wound and the subepithelial vascular tissue removes the possibility of the corneal epithelium proliferating into the anterior chamber." In 1948, Theobald [2] reemphasized this observation by stating:

> It is obvious from our observations that a wide conjunctival flap of equal width extending the entire circumference of the wound would remove the presence of the first requisite, i. e., the proximity of the proliferating edge of epithelium to the wound. . . . This . . . flap would make extremely rare the . . . possibility of an iris cyst resulting from implantion, for . . . an instrument would never pass into the anterior chamber through an epithelial surface.

With the exception of case 5, in which a conjunctival flap was fashioned superiorly, no conjunctival flap was made.

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20. In the first series, five doses of 150 r each were given at weekly intervals for six weeks, with the following technical factors: 250 kilovolts (peak), 0.5 mm. of copper filtration and a target-skin distance of 50 cm.

In the second series, five doses of 150 r were given at weekly intervals for six weeks, with the following technical factors: 108 kilovolts (peak), 3 mm. of aluminum filtration and a target-skin distance of 25 cm.

SUMMARY

Epithelial invasion of the anterior chamber is a most malignant postoperative complication of cataract extraction. The estimated incidence of this complication varies from 0.06 to 0.11 per cent. Conditions predisposing to the development of this complication are delayed formation of the anterior chamber and poor healing of the wound edges. The latter may be due to an intraocular hemorrhage, incarceration of iris, capsular remnants in the wound or prolapse of the vitreous.

In making the clinical diagnosis, this complication must be kept in mind. Given one of the aforementioned predisposing conditions together with the observation of the grayish haze on the posterior surface of the cornea which gradually progresses downward, the possibility of this complication is greatly strengthened.

If the epithelization is allowed to progress, the eye is inevitably lost through severe iridocyclitis and glaucoma. Any measure, therefore, which offers the slightest chance of arresting or retarding the development of this complication must be seriously considered. Operative intervention is of no avail. Application of the actual cautery to the fresh wound and the posterior surface of the cornea produced good results in the hands of Fazakas. Use of roentgen therapy (Perera) or the radon plaque (Vail) offers hope of retarding, arresting or even curing this condition.

The clinical history, type of operation, postoperative course and use of the radon plaque and roentgen radiation in 5 cases are reviewed. Retardation of the epithelial downgrowth was noted in 2 cases; definite recession took place in 1 case, and no improvement was noted in 1 case and the eye was enucleated four months after the cataract extraction. The pathologic report in this case corroborated the clinical diagnosis of epithelial invasion of the anterior chamber.

The time interval between the extraction of the cataract and the clinical recognition of epithelization of the anterior chamber in this series of cases varied from three weeks to five months.

Prevention, rather than treatment, should be one's aim. Use of the preformed conjunctival flap, 3 to 4 mm. in width, extending around the circumference of the wound, would eliminate the possibility of implantation of epithelium, as no instrument would pass into the anterior chamber through an epithelial surface.

TREATMENT OF GIANT FOLLICULAR LYMPHOMA WITH NITROGEN MUSTARD (METHYL-*BIS*-[2-CHLOROETHYL] AMINE)

Report of a Case

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PRIOR to 1927 the condition variously known as "giant lymph follicle hyperplasia of the lymph nodes and spleen," "giant follicular lymphadenopathy," "follicular lymphoblastoma," "Brill-Symmers disease" or "giant follicular lymphoma" was considered a benign disease. In that year Baehr and Rosenthal suggested that the condition be called "malignant lymph follicle hyperplasia." In 1931 Baehr, Rosenthal and Klemperer stated that the disease was a form of lymphosarcoma. They classified it as lymphoblastoma, characterized chiefly by (*a*) enlargement of lymph follicles and the spleen due to hyperplasia; (*b*) absence of changes in the cytologic elements of the blood; (*c*) occasional development of pleural and peritoneal effusions; (*d*) absence of involvement of the tonsils and lymphoid tissue of the gastrointestinal tract; (*e*) occasional unilateral exophthalmos resulting from lymphatic infiltration of the lacrimal gland, and (*f*) multicentric origin throughout the body in the lymph follicles, whereas lymphosarcoma arises monocentrically and spreads by lymphatic or hematogenous extension.

According to Willis,[1] it is now thought that giant follicular lymphoma may exist in either a benign or a malignant form. In the benign localized form there is slow enlargement of a single node. In the malignant form there is slow enlargement of one or more lymph nodes with extension to other nodes, leading ultimately to widespread disease. Both forms of the disease are rare. The malignant form, according to Mallory, has a survival rate of five to six years. In the descriptive case which Willis reported, death occurred in eight years after the appearance of the swollen node. At death, the patient had enlargement

Presented before the College of Physicians, Philadelphia, Section on Ophthalmology, March 17, 1949.

From the Graduate Hospital of the University of Pennsylvania, Department of Ophthalmology, Edmund B. Spaeth, M.D., Chief of Service.

1. Willis, R. A.: Pathology of Tumours, St. Louis, C. V. Mosby Company, 1948.

of the cervical, axillary, iliac and inguinal lymph nodes. According to Baggenstoss and Heck,[2] the average duration of life after the appearance of the disease is 4.5 years.

Usually, the lymph nodes of the neck show the earliest involvement, characterized by discrete enlargement and nontender, freely movable nodes. In more than one-half the reported cases there has been splenomegaly at some time. There is absence of evidence of chronic infection, such as pain, anemia and cachexia. The disease occurs most frequently in persons of the age group of 35 to 45 years. It is more prevalent in males than in females.

Pathologically, the lymph nodes show well differentiated lymphoid tissue, containing large follicles with germinal centers throughout. There is an increase in the number and size of the lymph follicles. The malpighian bodies in the spleen may show changes similar to those in the lymph nodes. The anatomic structure of the lymph node, including the capsule, remains intact. Because of the similarity of the histologic picture to that of chronic lymphadenitis, the disease is often diagnosed as such by pathologists.

The course of giant follicular lymphoma varies. There may be temporary spontaneous regressions with subsequent reappearance, or the disease may remain unchanged for months or years, only to be followed by, or transformed into, Hodgkin's disease, lymphosarcoma or leukemia.

Giant follicular lymphoma is very sensitive to roentgen radiation and radium. Irradiation is considered the most effective form of treatment. Uhlman,[3] in presenting a series of cases, stated that even though regression of the swelling may occur with doses as small as 300 to 400 r, this effect is only temporary and subsequent reappearance of the disease, with possible progression to Hodgkin's disease, lymphosarcoma or leukemia, may follow. He emphasized the ultimate development of malignancy of this condition and recommended early treatment with heavy doses of roentgen radiation.

During World War I, observers noted in mustard gas (2-chloroethyl sulfide) casualties that, in addition to the vesicant action on the skin, there were general systemic effects, indicated by leukopenia, anemia and gastrointestinal irritation. With renewed interest in gas warfare at the beginning of World War II, a large variety of mustard gas compounds were developed, including the chemical family known as

2. Baggenstoss, A. H., and Heck, F. J.: Follicular Lymphoblastoma (Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen), Am. J. M. Sc. **200**:17 (July) 1940.

3. Uhlman, E. M.: The Significance of Giant Follicular Lymphadenopathy (Brill-Symmers Disease), Radiology **50**:147 (Feb.) 1948.

nitrogen mustards, in which the sulfur is replaced by nitrogen. Of this family methyl-*bis*-(2-chloroethyl)-amine or *tris*-(2-chloroethyl)-amine are important members. Since nitrogen mustard was absorbed more readily than mustard gas, its selective systemic effects became more obvious. In experimental animals, nitrogen mustard was easily absorbed through the skin and reached high systemic concentrations, again calling attention to its cytotoxic effects in general and to its selective toxic effects on the hematopoietic, the lymphoid and the gastrointestinal systems in particular. There evolved the concept that since these agents had remarkably selective effects on certain rapidly growing tissues of the body, they might well represent a chemotherapeutic agent for the treatment of neoplasms of these systems. Attention was drawn to the similarity of the action of nitrogen mustard and the biologic effects of roentgen rays. For this reason, nitrogen mustard has been used in the treatment of a large variety of neoplastic diseases. It has shown its most pronounced effect on the lymphoma group. In Hodgkin's disease and lymphosarcoma there is usually an improvement in the patient's feeling of well-being, as well as a striking diminution in the size of the tumors. Although roentgen irradiation is considered the treatment of choice, nitrogen mustard offers added relief to those patients who have become resistant to roentgen rays.

Mainly, two nitrogen mustard compounds have been used, methyl-*bis*-(2-chloroethyl)-amine hydrochloride and *tris*-(2-chloroethyl)-amine hydrochloride. Rhodes [4] advised that the methyl-*bis* compound is to be preferred, as it is followed less frequently by venous thrombosis at the site of injection. It should be administered in an infusion of sodium chloride solution. The recommended dosage of a course is 0.1 mg. per kilogram of body weight given intravenously on four successive days. Additional injections may be given as indicated.

The toxic effects of nitrogen mustard are venous thrombosis at the site of injection, with severe local inflammatory reaction if the material escapes into the tissues; nausea and vomiting, and damage to blood-forming organs, with varying degrees of leukopenia, anemia and thrombocytopenia.

The case to be presented represents the malignant form of giant follicular lymphoma. Certain features made the decision to use nitrogen mustard therapy somewhat unusual.

REPORT OF CASE

H. K., a white bricklayer aged 64, noticed a swelling in the region of the inner corner of his right eye in May 1948. The enlargement gradually involved both the upper and the lower lid. Vision was not impaired. He was examined by

4. Rhodes, C. P.: Nitrogen Mustards in Neoplastic Disease, J. A. M. A. **131**:8 (June 22) 1946.

several ophthalmologists and otolaryngologists in his home town and was referred to a hospital in Philadelphia for diagnosis and treatment. In September biopsy of tissue removed from the anteromedial aspect of the right orbit through an incision in the upper lid was reported as showing probable rhabdomyosarcoma. A routine roentgenogram of the chest revealed a large mediastinal mass. The patient was transferred to the Graduate Hospital on September 27 for investigation of this mass.

On admission, there was almost complete ptosis of the right upper lid with obliteration of the lid fold, due to an enlargement in that region. There was no exophthalmos or involvement of the third or seventh nerve. On palpation, a firm, nontender, nonfluctuant area could be felt along the lateral half of the upper lid. Parallel and inferior to the brow along the medial aspect of the upper lid was a surgical scar resulting from the previous biopsy. There was impairment of rotation of the right eye medially and superiorly. The palpebral conjunctiva was injected. Except for floaters in the vitreous, examination of the right eye showed nothing noteworthy. Examination of the left eye revealed no abnormality. Vision was 6/22 in the right eye and 6/30 in the left eye. Tension was 22 mm. in the right eye and 22 mm. in the left eye. The family, social and past medical histories were without significance.

Fig. 1.—Appearance of patient on admission to hospital. The biopsy scar and displacement of the right eye are apparent.

Examination of the head, excluding the right orbit, revealed nothing abnormal. In the left posterior cervical region of the neck could be felt several slightly enlarged, nontender, movable lymph nodes. No other lymph nodes were palpable. The lungs were clear to percussion and auscultation. The blood pressure was 150 systolic and 85 diastolic in the right arm and 140 systolic and 90 diastolic in the left arm. The heart was not enlarged; the rate, rhythm and sounds were normal. There was a soft systolic murmur in the aortic area. Examination of the abdomen revealed a direct inguinal hernia on the right side. There were no palpable masses in the abdomen. The liver and spleen were not felt. The extremities were normal. The cytologic and chemical constituents of the blood and the bone marrow were normal. The Wassermann reaction of the blood was 4 plus; that of the spinal fluid was 4 plus, with a first zone colloidal gold curve (1543321000).

Bronchoscopic examination showed a normal condition on two occasions. Examination of the genitourinary tract revealed nothing abnormal. The electrocardiogram was normal.

Roentgenologic studies of the skull revealed a slight increase in density over the right orbit, thought to be due to swelling of the soft tissues. No bony defects

were noted. A roentgenologic report on the chest stated that the cardiovascular silhouette showed partial imposition of a large, round, dense mass, measuring about 7.5 cm. in diameter, in the midpart of the anterior mediastinum. Repeated roentgenologic examinations failed to identify the nature of the mass. It was thought by members of the roentgenology department to be either an aneurysm or a dermoid. Roentgenograms of the pelvis revealed nothing remarkable.

On October 13 biopsy of a cervical lymph node was reported as showing giant follicular lymphoma.

On November 4 a piece of tumor measuring about 1 by 1 by 3 cm. was removed through an incision in the lateral aspect of the right upper lid. The microscopic diagnosis was lymphoma, probably malignant. No mention of the presence of lacrimal gland tissue in the orbital tumor was made in any of the pathologic reports.

Beginning on October 6, the patient was given antisyphilitic treatment in the form of 600,000 units of penicillin daily for a period of ten days.

From October 20 to October 28, 1,500 r was given over the anterior mediastinum, without any visible effects on the mediastinal mass. The possibility of irradiation of the right orbit was considered and rejected, since it was thought

Fig. 2.—Appearance of patient four months after administration of nitrogen mustard.

that the orbital tumor was part of a generalized malignant process on which roentgen radiation had shown no effect, and the use of which would result in damage to a comparatively normal eye. Sacrifice of the right eye by exenteration of the orbit was not thought justifiable, since it would not change the prognosis.

Beginning on November 22, the patient was given 6.2 mg. of methyl-*bis*-(2-choroethyl)-amine hydrochloride on four successive days, without reaction. Within three days after the completion of the course of nitrogen mustard injections, a marked diminution of the swelling in the region of the right orbit was noted. There was simultaneous regression in the size of the cervical lymph nodes.

When the patient was dismissed from the hospital, on December 7, there had been a complete remission of his orbital signs and symptoms. Since leaving the hospital, he has been followed regularly by the ophthalmology and roentgenology departments. When last seen, four months after the completion of nitrogen mustard therapy, there was no evidence of reappearance of giant follicular lymphoma. Vision has remained unchanged.

The last roentgenologic examination of the chest showed no change from the condition seen on his first examination, made six months previously. Although the nature of the mediastinal mass has not been definitely determined, in view of

its lack of response to roentgen and nitrogen mustard therapy, in all probability it is not a lymphoma. Considering the presence of latent syphilis, one may postulate that the mass is an aortic aneurysm.

COMMENT

Should nitrogen mustard (methyl-*bis*-[2-chloroethyl]-amine) ultimately prove to be no more effective than roentgen radiation in the treatment of giant follicular lymphoma, its use avoids the hazards of irradiation on the eye. For this reason, it may be of particular interest to ophthalmologists.

ABSORPTION OF PROTEIN THROUGH THE CONJUNCTIVAL MUCOUS MEMBRANE

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THERE are many reports of systemic poisoning resulting from the absorption of drugs instilled into the eyes. Symptoms have followed the instillation of cocaine and atropine into the conjunctival sac.

It has not always been certain whether such absorption occurred through the mucous membrane of the conjunctiva or through the nasal mucous membrane after the drug had reached the nose by way of the nasolacrimal duct. Macht [1] ligated or cauterized the nasolacrimal ducts of dogs and was able still to elicit the central actions of morphine and apomorphine after their instillation into the eye. Other drugs studied through their pharmacologic responses in animals [2] include aconitine, nicotine, potassium cyanide, cocaine, pilocarpine and potassium iodide.

There are no reports in the literature on the absorption of protein through the conjunctival mucosa. It is the purpose of this study to demonstrate, by immunologic means, that unaltered protein may be absorbed through the conjunctival mucous membrane of the human eye.

It has been shown by Walzer and his associates [3] that a cutaneous site which has been passively sensitized to an allergen will react after the systemic absorption of that allergen through various portals of entry. Absorption has been experimentally demonstrated through the mucous membranes of the alimentary tract, the nose,[4] the urinary bladder [5] and

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From the Allergy Division of the Jewish Hospital of Brooklyn.

1. Macht, D. I.: Absorption of Apomorphine and Morphine Through Unusual Channels, Proc. Soc. Exper. Biol. & Med. **15**:26, 1917.

2. Macht, D. I.: Absorption of Drugs Through the Eye, Ear, Teeth, and Esophagus, J. Pharmacol. & Exper. Therap. **22**:123, 1923.

3. Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings: I. A Simple Direct Method of Studying the Absorption of Undigested Protein, J. Immunol. **14**:143, 1927; Absorption of Allergens, J. Allergy **13**:554, 1942.

4. Chait, R. A., and Walzer, M.: Absorption of Unaltered Protein Through the Nasal Mucous Membrane: I. Technic, to be published.

5. Baretz, L. H.; Harten, M., and Walzer, M.: The Absorption of Protein from the Urinary Bladder, J. Urol. **50**:71, 1943.

the vagina and cervix uteri.[6] In the present study, the same technic was employed to demonstrate the absorption of protein from the conjunctival sac.

PRESENT INVESTIGATION

Subject.—A Negro girl aged 6 years, who at the age of 2 years had undergone extirpation of her lacrimal sacs for chronic dacryocystitis, was the subject of this experiment. She gave no personal history of allergy, but her mother had hay fever, and another sibling had eczema. A skin test with peanut extract gave negative results. The eyes were normal except for the presence of epiphora.

The Sensitizing Serum.—The serum for sensitization was obtained from a patient who was extremely sensitive to peanuts. The titer of the reagins for peanut in this serum was high (1:1,024, determined by the dilution method of Coca and Grove[7]). Reagins for other antigens, such as peas, beans, nuts and mustard, were present in this serum in low titer.

Passive Local Sensitization.—Passive local sensitization of the subject was induced by the intracutaneous injection of 0.05 ml. of the sensitizing serum on the upper and outer aspect of the arm. For twenty-four hours prior to sensitization, and until the time of testing, peas, beans, nuts and mustard were excluded from the subject's diet.

The Antigen.—The antigen used for the absorption test was an extract of peanut prepared according to the method of Coca and Milford,[8] with a nitrogen content of 0.5 mg. per milliliter.

The Absorption Test.—The test for absorption was performed twenty-four hours after sensitization. A small pledget of cotton, soaked in the extract of peanut, was introduced into the lower conjunctival sac and was moistened at frequent intervals with the same extract. Slight congestion of the conjunctiva resulted from this procedure.

Result.—Twenty-one minutes after the introduction of the allergen into the conjunctival sac, a reaction appeared at the sensitized cutaneous site. Intense pruritus was rapidly followed by a marked erythema and a large wheal, 7 cm. in diameter. This cutaneous reaction demonstrated the passage of the peanut allergen through the conjunctival mucous membrane into the circulation.

COMMENT

Since antigenic proteins and drugs may be rapidly absorbed through the conjunctival mucous membrane, eye drops may produce allergic systemic reactions. In this study, on a subject with occluded nasolacrimal ducts, absorption of protein occurred only from the conjunctival mucous membrane. In normal persons with patent nasolacrimal ducts, allergens instilled into the conjunctival sac may also reach the nose, where

6. Rosenzweig, M., and Walzer, M.: The Absorption of Antigen from the Vagina and Cervix in Humans, Am. J. Obst. & Gynec. **75**:286, 1943.

7. Coca, A. F., and Grove, E. F.: Studies in Hypersensitiveness: XIII. A Study of the Atopic Reagins, J. Immunol. **10**:445, 1925.

8. Coca, A. F., and Milford, E. L.: Studies in Specific Hypersensitivities: XVII. The Preparation of Fluid Extracts and Solution for Use in the Diagnosis and Treatment of Atopic Conditions, J. Immunol. **10**:555, 1925.

absorption of proteins normally occurs.[9] The potential absorptive area which may be reached by eye drops is, therefore, much greater than the conjunctival mucous membrane alone. Hence, the conjunctival sac as a possible entry for allergenic excitants should not be underestimated.

SUMMARY

The rapid absorption of protein through the human conjunctival mucous membrane is demonstrated with an immunologic technic.

Dr. Bernard Welt, of the Department of Otolaryngology, made available the patient with obliterated nasolacrimal ducts.

20 Plaza Street (17).

9. Chait and Walzer.[4] Cohen, M. B.; Ecker, E. E.; Breithart, I. R., and Rudolph, I. A.: The Rate of Absorption of Ragweed Pollen Material from the Nose, J. Immunol. **18**:419, 1930.

OBJECTIVE TESTING OF VISION WITH USE OF THE GALVANIC SKIN RESPONSE

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IN THE experiments reported here, the aim is to outline a simple technic for the objective testing of vision. This technic has been found useful as an aid in the diagnosis of psychogenic factors or of malingering in visual defects in man, whether the defects are present as a failure of visual acuity or as a limitation of the visual field, and, with modifications, can also be used for the study of vision in animals.

This objective testing is made possible by use of a skin galvanometer that gives a graphic record of activity in the sympathetic nervous system. The galvanometer records a phenomenon that was first described by Féré [1] in 1888 and by Veraguth and Müller (Veraguth [2]) in 1904, and has since become known either as the psychogalvanic or, more simply, as the galvanic skin response. Féré showed that in hysterics a variety of excitations—visual, auditory, gustatory, olfactory and emotional—decrease the resistance that the body offers to the passage of a minute direct electric current. It has since been shown that normal subjects show the same response.

It has also been demonstrated (1) that changes in resistance are localized in the skin and not in the rest of the body; (2) that this phenomenon depends on the intactness of the sympathetic nervous system, and (3) that it has a latency period of one or two seconds, indicative of a neuroglandular transmission mechanism, rather than any involvement of striated muscle.

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* Henry Strong Denison Scholar for 1949-1950.

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The work described in this paper was done under a grant from the Office of the Surgeon General of the United States Army to the Johns Hopkins University (Dr. C. P. Richter).

1. Féré, C.: Note sur des modifications de la résistance électrique sous l'influence des excitations sensorielles et des émotions, Compt. rend. Soc. de biol. **5**:217, 1888.

2. Veraguth, O.: Das psychogalvanische Reflexphänomen, Berlin, S. Karger, 1909.

The skin galvanometer was developed by Richter and Whelan in this laboratory and has been described in detail by them.[1] The instrument consists of a General Radio Company direct current amplifier; a 5 milliampere ink-recording ammeter, Esterline-Angus model; a control panel; a 4½ volt battery, and electrodes. The electrodes, coated with a paste of kaolin and a saturated zinc sulfate solution, are attached to the palm and back of the patient's hand. The wiring is essentially a Wheatstone bridge circuit. The ratio arms *P* and *Q* in their diagram,[1] consist of 150,000 ohm fixed resistors. The patient is connected as the *X* arm, and, by means of two rheostats, which are connected as the *R* arm, the bridge is balanced by bringing the galvanometer to the zero point on the indi-

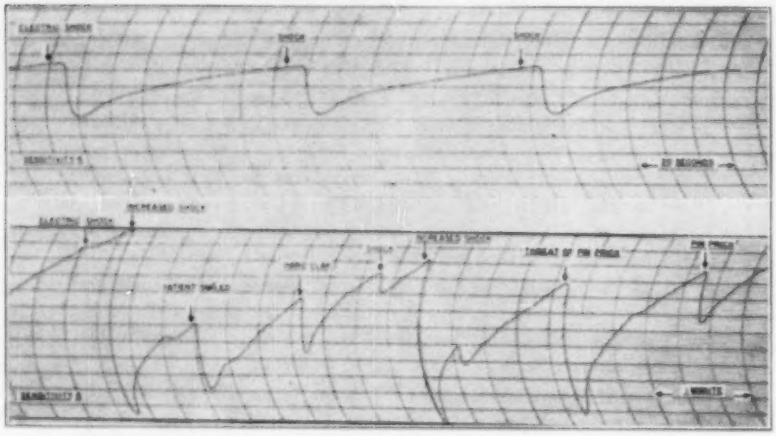

Fig. 1.—Typical record of changes in electrical skin resistance in man produced by the stimuli indicated. The sensitivity refers to the setting of the input resistance of the amplifier, ranging from 1 to 7.

cator, that is to the midpoint of the recorder. This is the base line for the recording. The changes in the patient's skin resistance unbalance the bridge and cause currents to flow through the amplifier. These currents can be amplified to various degrees by the amplifier and recorded in ink on the recorder. Figure 1 shows a typical human record, responses to electric shocks, hand claps, pinprick and threat of pinprick being indicated. The downward deflection indicates the response, namely, a decrease in the electrical skin resistance. At the lower left of the

1. Richter, C. P., and Whelan, F. G.: Description of a Skin Galvanometer That Gives a Graphic Record of Activity in the Sympathetic Nervous System, J. Neurosurg. **6**:279 (July) 1949.

records is indicated the level of sensitivity of the amplifier, which ranged from low to high amplification in seven steps.

Our experiments with visual testing were suggested by the technic of Drs. Bordley, Hardy and Richter in objective testing of hearing in human beings.[4] They recorded galvanic skin responses to various pure tones of varying intensity after the patient has been conditioned to expect an electric shock whenever a tone was sounded.

This recording of the galvanic skin response is also a basis for the objective testing of vision. The technic is illustrated in figure 2. The patient whose visual acuity is to be tested sits in a chair connected with the psychogalvanometer by electrodes attached to the palms of the hands.

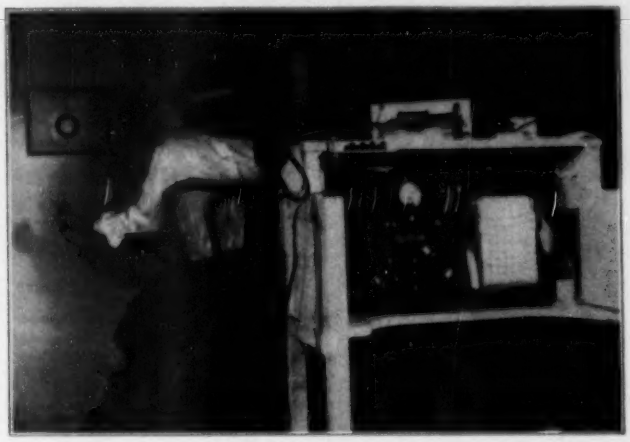

Fig. 2.—Patient whose visual acuity is to be tested connected with the psychogalvanometer.

An electric shock can be given by means of electrodes attached to the leg and connected to a Harvard inductorium. The patient faces a screen on which letters of variable sizes can be projected, one at a time, using an American Optical Company project-o-chart.[5] In the case of adult patients, it is first explained to the subject that a certain letter, E, for example, will be followed by an irritating faradic shock and that no other letter of the alphabet will be followed by this shock. With some adults, and with most children, a conditioned response to the single

4. Bordley, J. E.; Hardy, W. G., and Richter, C. P.: Audiometry with the Use of Galvanic Skin-Resistance Response, Bull. Johns Hopkins Hosp. **82**:569, 1948.

letter cannot be satisfied by this statement alone, and therefore the conditioning procedure is carried out until the patient has been conditioned to respond to the given letter.

By projecting the standard eye chart, one letter at a time, and passing the visual threshold in both directions, one obtains the visual acuity of the patient by observing the wave of the psychogalvanometer. Figure 3 is a portion of an actual record of a patient. It shows the large response

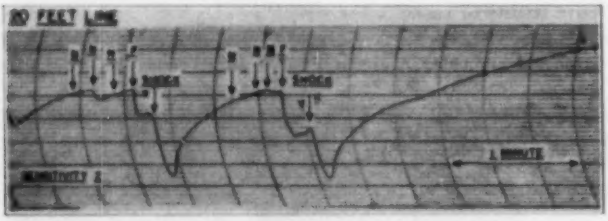

Fig. 3.—Part of an actual record of a patient whose visual acuity was tested. *N* indicates response for a neutral letter; *F*, response to a conditioned letter.

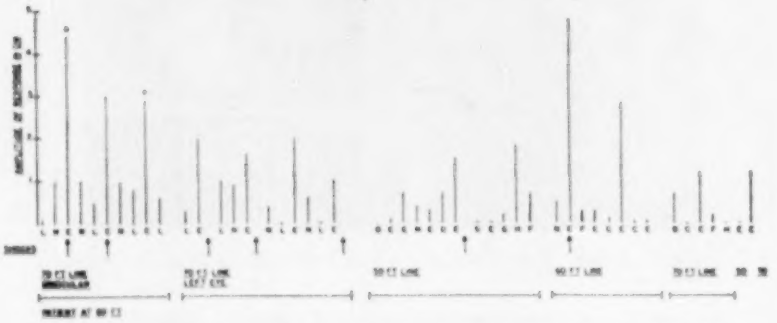

Fig. 4.—Graph of an entire record (galvanic skin response) of a patient who claimed to have total blindness in the left eye.

which the patient gave when the conditioned letter was flashed on the screen. Figure 4 is a chart on which is presented an entire record of responses from a patient who complained of total blindness of the left eye. The ordinate shows the amplitude of the response obtained by presenting the letter shown on the abscissa. A deflection of 1 cm. equals a change in skin resistance of approximately 10,000 ohms. The electric shocks were given either one second after the letter was flashed (indicated by the arrow under the letter) or five seconds after

the letter was flashed (indicated by the arrow following the letter). In the latter case, the response to the letter alone is obtained. This patient was applying for a pension at the Perry Point Veterans Hospital. As soon as he had been conditioned, using both his good and his bad eye, the letters were flashed before his bad eye alone. He gave a response each time a letter was flashed, although he had absolutely no way of knowing when the letter was flashed other than by seeing it. Moreover, when the conditioned letter E appeared, he gave very large responses. As the letters diminished in size—the 50 foot (15 meter) line—the responses indicated that he was not certain what the letter was. He responded greatly to H, and several times did not give a large response to the conditioned letter. The responses along the 60 foot (18 meter) line were also inconsistent. Returning to the 70 foot (21 meter) line, the patient once again responded to the conditioned letter. Thus the record presents evidence that the patient could distinguish letters on the 70 foot line and that therefore there was some psychogenic involvement in his blindness.

In objective perimetry, the patient is attached to the psychogalvanometer in the same position as is used in subjective perimetry. The first step is to condition the patient to expect an electric shock whenever he sees the white target dot. This is done by presenting the white dot to that part of the field where the patient says that he can see, and following this presentation by application of the electric shock. After the patient has been conditioned to give a galvanic response at the sight of the dot, the dot is moved slowly into his field from the periphery. When the patient sees the dot, the response is indicated on the psychogalvanometer. The dot must be moved slowly, since there is a latent period of approximately two seconds between the stimulus and the start of the response.

Visual acuity was studied by this method in 4 children, with ages ranging from 5 to 13 years; in 3 patients with malingering or hysterical blindness; in 5 patients at the Wilmer Ophthalmologic Clinic, Johns Hopkins Hospital, and in 7 normal subjects. At the time of this report objective perimetric studies have been made on only 1 person.

Objective visual testing is of assistance to the physician when confronted by patients who are believed to have some psychogenic involvement, especially in military service and in compensation cases. With animals, this objective testing is essential, since it is impossible to obtain a vocal report of an animal's sensory perception. For this reason, we wish to present a modified technic of the type described for human beings which will make possible studies of visual acuity and visual field in animals. Monkeys, cats and rats were used as experimental

animals. The presence in monkeys and cats of sweat glands on the pads of the feet is well known. Recently, Ring and Randall [5] described sweat glands in the foot pads of the rat.

Two difficulties present themselves when one attempts to carry the technic directly from man to animals: 1. The animal must remain relatively motionless in order that the electrodes may be attached to the pads of the feet and that muscular contraction, which interferes with the recording of the galvanic skin responses, may be prevented. 2. The animal's head must face a screen on which letters are projected, and, for perimetric studies, the animal must fix its eyes on a point straight ahead. To solve these difficulties, physical restraint of various types

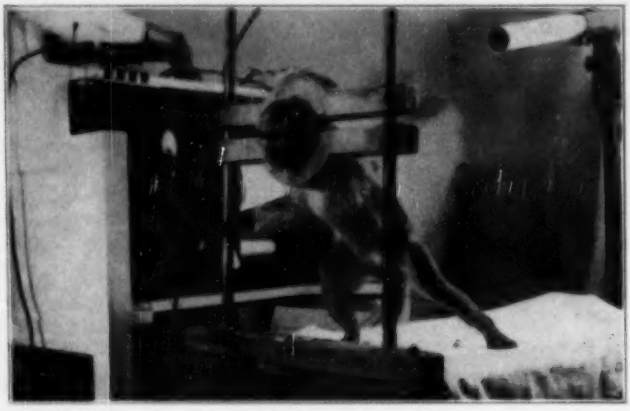

Fig. 5.—A monkey prepared for visual studies. The galvanic skin response was recorded from electrodes attached to the soles of the hindfeet. Electric shocks were given through the bars which the monkey grasps.

was attempted, without success. Therefore, we had to look elsewhere for a possible solution to those problems. Previous reports from this laboratory have described the use of a drug which immobilizes an animal to the extent that complex surgical procedures can be performed with the drug given in conjunction with a local anesthetic.[6] Moreover, with

5. Ring, J. R., and Randall, W. C.: The Distribution and Histological Structure of Sweat Glands in the Albino Rat and Their Response to Prolonged Nervous Stimulation, Anat. Rec. **90**:7, 1947.

6. Levine, M., and Wolff, H. G.: Cerebral Circulation, Arch. Neurol. & Psychiat. **28**:140 (July) 1932.

the use of the drug, the animal remains alert to sensory stimuli of all types. This drug, an alkaloid obtained from Corydalis cava, is called bulbocapnine; it produces a cataleptic state in animals sometimes referred to as experimental catatonia because of its similarity to that syndrome in man.[7]

The use of this drug produces the immobility and fixed gaze which is needed for studies of vision with the galvanic skin response. Figure 5 shows a monkey prepared for visual studies. The immobility is produced by injection of 15 mg. per kilogram of body weight. We have

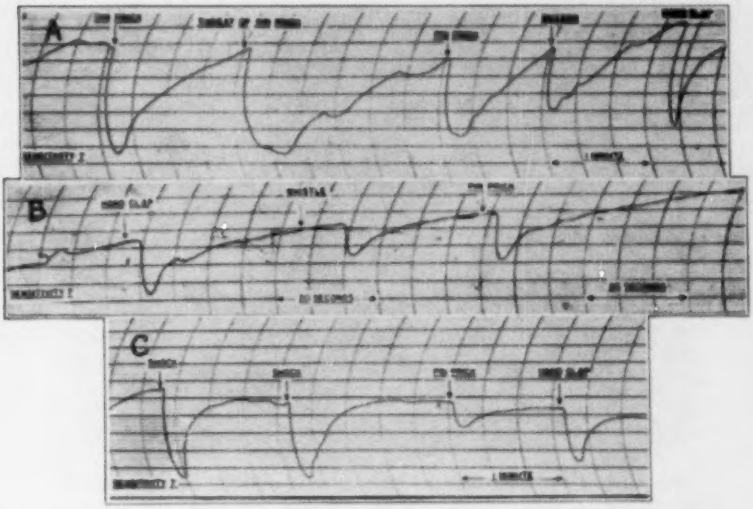

Fig. 6.—Galvanic skin responses obtained while the animals (*A*, monkey; *B*, cat; *C*, rat) were in a state of bulbocapnine-induced catalepsy.

recorded responses over a five hour period, with the animal in one position.

Figure 6 shows responses of a monkey, cat and rat obtained while the animals were in a state of bulbocapnine-induced catalepsy. The similarity to the record of a normal human subject is striking. That the responses in animals represent sympathetic activity similar to

7. Ferraro, A., and Barrera, S. E.: Experimental Catalepsy, New York, State Hospitals Press, 1932. DeJong, H. H.: Experimental Catatonia, Baltimore, Williams & Wilkins Company, 1945.

the responses obtained in man, is demonstrated by the following experimental results:

1. Electrical stimulation of the surgically exposed sympathetic nerve chain in monkeys and cats produces similar responses, i. e., similar decreases in skin resistance.

2. In chronic preparations (rats with unilateral lumbar sympathectomy) responses to stimuli are absent when galvanic skin responses are recorded from the side of operation, whereas these responses are present when recorded from the normal side. Figure 7 is a record obtained from one of these rats.

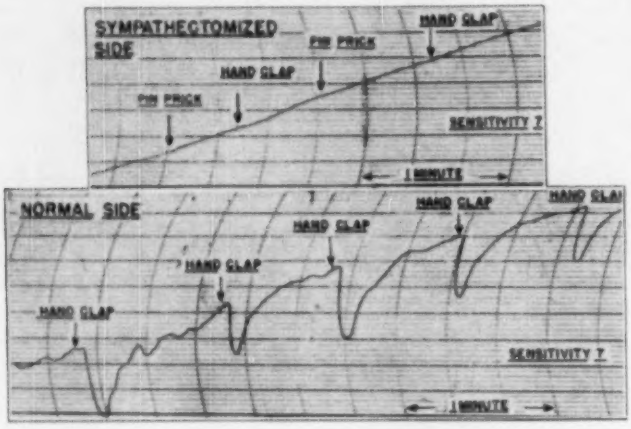

Fig. 7.—Galvanic skin responses from a rat with unilateral lumbar sympathectomy while the animal was under bulbocapnine-induced catalepsy.

3. In the monkey, cat and rat there is a definite latency period between the stimulus and the start of the response, similar to that recorded in human beings. For these reasons, we believe that the phenomenon in the monkey, cat and rat is the same as that in man.

SUMMARY

With use of the conditioned galvanic skin response, and, in the case of animals, the catalepsy-producing drug bulbocapnine, an attempt has been made to present a technic for the objective testing of vision in man, monkey, cat and rat.

Mrs. William Dinsmore assisted in the preparation of the illustrations.

EARLY DIAGNOSIS OF SYPHILITIC PRIMARY OPTIC NERVE ATROPHY

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IN A PREVIOUS communication [1] a study of 397 patients with syphilitic primary optic nerve atrophy was presented. The visual acuity of 61 per cent of these patients when they were first seen was less than 6/60 in both or in the better eye (in 44 per cent it was 1/60 to 6/60, and in 17 per cent it was less than 1/60). This constitutes industrial blindness and represents an unfortunate experience in the early diagnosis of syphilitic optic nerve atrophy among the ward and clinic patients at Wills Hospital.

Our purpose in the present paper is to discuss the earliest signs of syphilitic optic nerve atrophy, the prodromal symptoms and the pitfalls in early diagnosis.

Pertinent data in the study of our 397 patients in relation to early diagnosis are concerned with the following points: 1. The occurrence of optic nerve atrophy in patients whose early syphilis was untreated. 2. The number of patients who had no knowledge of infection and no previous serologic tests for syphilis. The complaint of impaired visual acuity was frequently the first and only symptom that motivated medical consultation. 3. The lack of ophthalmologic examination of patients who consulted physicians or clinics in what was presumably the predromal or prodromal stage of the disease, with subjective impaired visual acuity. Thirty-one per cent of the patients [2] at the onset of visual loss consulted an optometrist for their initial treatment.

From the Clinic for Treatment of Ocular Syphilis, Wills Hospital.

Read at the First Annual Clinical Conference of Wills Hospital, May 6, 1949.

The work described in this paper was done under a contract recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Wills Hospital, and later under a grant-in-aid from the Research Grants and Fellowship Division, National Institute of Health, United States Public Health Service.

1. Klauder, J. V.; Meyer, G. P., and Gross, B. A.: Syphilitic Primary Optic Atrophy as a Cause of Blindness: Importance of Early Diagnosis, Am. J. Syph., Gonor. & Ven. Dis. **32**:574, 1948.

2. These figures were obtained by Lehrfeld and Gross (Am. J. Ophth. **21**: 435, 1938) in a study of syphilitic optic nerve atrophy in patients attending Wills Hospital.

Syphilitic primary optic nerve atrophy occurs in association with all forms of neurosyphilis of acquired and of congenital syphilis. From pathologic studies, Bruetsch [3] observed syphilitic optic nerve atrophy occurring as a focal form of neurosyphilis without other pathologic evidence of neurosyphilis. Clinically, however, we have rarely observed optic nerve atrophy in a syphilitic patient who had no neurologic abnormalities of neurosyphilis and whose spinal fluid gave no evidence of the disease. The disease is seen more frequently in association with tabes or the tabetic form of dementia paralytica, although Bruetsch,[3b] on the basis of anatomic investigation, did not observe any great difference in its incidence in tabes and in dementia paralytica.

The incidence of optic nerve atrophy in patients with the tabes of acquired syphilis is generally stated to be 10 to 15 per cent. The interval between infection and onset of optic nerve atrophy is rarely less than ten years, the average being eighteen years. The predominating age for patients with acquired syphilis is 40 to 50 years, and that for patients with congenital syphilis, 15 to 25 years. The incidence of optic nerve atrophy is greater in white persons than in Negroes (57 per cent, as compared with 43 per cent, in our series). The disease, however, is more frequent among neurosyphilitic Negroes of both sexes than among neurosyphilitic white patients.[4] Males are more affected than females, the ratio varying from 3.5 or 5.5 to 1, as reported by different investigators.

An important consideration in early diagnosis is the considerable percentage of our patients whose underlying neurosyphilis pursued a silent course so far as subjective symptoms were concerned. As has been pointed out by others, optic nerve atrophy associated with the tabetic form of neurosyphilis rarely occurs in what is called inferior, or "leg," tabes, in which is present the triad of tabetic symptoms—lightning pains, dysuria and ataxia. In our series of patients it was unusual to observe bladder disturbance, visceral crisis, arthropathy, headache, "nervousness," pain of radiculitis or other subjective symptoms of diffuse meningovascular neurosyphilis, or paralysis of one or more of the oculomotor muscles.

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3. Bruetsch, W. L.: (*a*) Malaria Therapy in Syphilitic Primary Optic Atrophy, J. A. M. A. **130**:14 (Jan. 15) 1946; (*b*) The Frequency of Syphilitic Primary Optic Atrophy in General Paralysis: A Clinico-Anatomical Study, Am. J. Psychiat. **104**:725, 1948; (*c*) Unilateral Syphilitic Primary Atrophy of the Optic Nerves, Arch. Ophth. **39**:80 (Jan.) 1948; (*d*) Surgical Treatment of Syphilitic Primary Atrophy of the Optic Nerves (Syphilitic Optochiasmatic Arachnoiditis), ibid. **38**:735 (Dec.) 1947.

4. Moore, J. E.; Hahn, R. D.; Woods, A. C., and Sloan, L.: The Treatment of Syphilitic Primary Optic Atrophy, Am. J. Syph., Gonor. & Ven. Dis. **26**:407, 1942.

In addition to the complaint of impaired visual acuity, the most frequent prodromal symptoms of optic nerve atrophy were pain in the legs and diplopia. Pain in the legs was typical of the tabetic type, being stabbing, or lancinating, and occurring and recurring in "crises." It was usually not incapacitating or sleep disturbing. It antedated by long periods subjective visual loss, and with many patients the history of pain was elicited only on questioning. This was true, too, of diplopia, which was usually transitory and invariably preceded, frequently by years, the complaint of visual loss.

Some patients, in addition to optic nerve atrophy and positive reactions of the spinal fluid, had pupillary changes as the only neurologic abnormality. Such a form has been designated as "optic tabes" or "preataxic optic atrophy," and its diagnosis illustrates the difficulty of classifying the type of neurosyphilis associated with optic nerve atrophy. The pupils, however, were hardly ever normal. The most constant findings in our series of patients, in addition to optic nerve atrophy, were positive serologic reactions of the blood and spinal fluid for syphilis and pupillary abnormalities—inequality, irregularity, sluggishness in reaction to light, Argyll Robertson pupil and fixation to light and in accommodation. As is well known, pupillary abnormalities are among the earliest and most constant signs of neurosyphilis, preceding by years the appearance of subjective symptoms. Their detection constitutes a "short cut" to the clinical diagnosis of neurosyphilis. Determination of the state of the pupils is of great importance in examination of a syphilitic patient whose disease has progressed beyond the early stage of infection and should aid in the early diagnosis of optic nerve atrophy.

PATHOLOGY OF SYPHILITIC PRIMARY OPTIC NERVE ATROPHY

Comprehensive reviews of the primary phase of optic nerve atrophy have been published by Moore,[5] Schiff-Wertheimer[6] and Moore and Woods.[7]

Moore and Woods stated that there is general agreement among pathologists that the process begins in the intracranial portion of the optic nerve distal to the chiasm. There are thickening and perivascular round cell infiltration of the overlying membranes, especially the pia, and of the connective tissue septums of the nerve, and this degeneration occurs first in the marginal fibers of the nerve. There is, however, no agreement as to the important question of the relation, if any, of the

5. Moore, J. E.: The Syphilitic Optic Atrophies, with Especial Reference to Primary Optic Atrophy, Medicine **11**:263, 1932.

6. Schiff-Wertheimer, S.: Pathogénie et traitement de l'atrophie optique tabétique, Bull. Soc. d'opht. de Paris, 1932, no. 8, pp. i-XCiX.

7. Moore, J. E., and Woods, A. C.: The Pathology and Pathogenesis of Syphilitic Primary Optic Atrophy, Am. J. Ophth. **23**:1, 1940.

inflammatory changes in the membranes and septums to the degenerative process in the nerve, since the former are frequently found in neurosyphilitic patients who do not show the latter change.

From pathologic studies, Behr [8] envisaged the disease as occurring in two forms: (1) an inflammatory form with secondary degeneration of the nerve fibers, and (2) primary degeneration in the form of tabetic atrophy of the nerve. Still other investigators postulated a form with basilar meningitis and a tabetic form of syphilitic optic nerve atrophy.

Since the review of Moore and Woods [7] (1940), the most notable pathologic study of syphilitic optic nerve atrophy has been made by Bruetsch.[8] The employment of modern methods of staining and their use with alternating serial sections permitted the simultaneous observation of both the inflammatory and the degenerative phase of syphilitic optic nerve atrophy.

Apparently, Bruetsch, more clearly than any other investigator, has visualized an inflammatory exudative phase preceding degenerative changes. According to Bruetsch, the principal site of the inflammatory pathologic process is in the intracranial portion of the optic nerves or in the chiasm or in both and is dependent on a varying degree of syphilitic basilar meningitis. The inflammatory lesion in the optic nerves and chiasm consists of cellular infiltrations in the septal connective tissue and around the blood vessels. As these exudative processes become extensive, demyelination (atrophy) of the nerve ensues, which in the majority of instances begins in the outer margins, where the syphilitic inflammation is most pronounced. Bruetsch stated the opinion that visual field defects may be caused by exudative processes in the marginal zone before atrophy of the nerve fibers has taken place and that such defects may improve or disappear after antisyphilitic treatment. This is not to be expected, however, if degeneration was present at the time of therapy.

Bruetsch observed no difference in the pathologic process of optic nerve atrophy in dementia paralytica and in the tabetic form of the disease; indeed, he noted no great difference in the incidence of optic nerve involvement in the two diseases. His studies supported only the inflammatory pathogenesis of optic nerve atrophy. He stated the belief that the clinical dictum of the greater frequency of optic nerve atrophy among patients with tabes and the tabetic form of dementia paralytica is more apparent than real and is related to diagnostic discrepancies in the clinical classification of neurosyphilis, the failure of clinical recognition of the condition in persons with dementia paralytica and a shorter

8. Behr, C.: (*a*) Syphilis und Sehnerven, Med. Welt. **12**:1515, 1938; (*b*) Das Verhalten und die diagnostische Bedeutung der Dunkeladaptation bei den verschiedenen Erkrankungen des Sehnervenstammes: II. Die atrophischen Zustände des Sehnerven, Klin. Monatsbl. f. Augenh. **55**:449, 1915.

span of life of these patients. The observation that only a certain number of patients with neurosyphilis have optic atrophy he explains by the considerable variation in the intensity of the pathologic processes in different regions of the brain and its meninges, the optic chiasm and the meninges of structures adjacent to the chiasm.

EARLY OPHTHALMOLOGIC DIAGNOSIS

The following changes have been reported by various authors as the earliest evidence of syphilitic optic nerve atrophy: loss of dark adaptation; visual field defect, preceding loss of central vision and pallor of the optic nerve (such a field defect may comprise a paracentral scotoma, enlargement of the blindspot or contraction of the peripheral visual fields); loss of the field for color, particularly red and green, and pallor of the optic disk.

The older ophthalmologists, notably Behr,[8] emphasized loss of dark adaptation as an early symptom. We know of no study of loss of dark adaptation as determined by modern methods in patients with early syphilitic optic nerve atrophy. We have had no experience. In any event, we do not regard as practical consideration of the presence of loss of dark adaptation as a means of early diagnosis.

Igersheimer,[9] Fuchs,[10] Paton,[11] Berger[12] and Sloan and Woods[13] reported a variety of field defects (such as are shown in figures 1 to 6) occurring in the absence of pallor of the disks and loss of central vision. Fuchs[10] stated the opinion that a central scotoma may first be demonstrated only for red and green.

Demonstration of a scotoma, enlargement of the blindspot and loss of function for color as early evidences of optic nerve atrophy necessitate tangent screen and perimetric determinations with white, red, green, blue and yellow test objects of several sizes each in order to secure a quantitatively accurate picture. The desirability of such a procedure cannot be questioned, but the practicability and reliability of results with some patients are open to question. Such studies require the time (one to two hours) and patience of a skilled operator, preferably an ophthalmologist. Moreover, the average patient, particularly the clinic type, has neither the patience nor the discriminatory acumen necessary

9. Igersheimer, J.: Syphilis und Auge, in Jadassohn, J. P.: Handbuch der Haut- u. Geschlechtskrankheiten, Berlin, Julius Springer, 1928, vol. 17, pt. 2, pp. 312-350.

10. Fuchs, E.: The Field of Vision in Tabetic Atrophy of the Optic Nerve, Tr. Am. Ophth. Soc. **12**:718, 1911.

11. Paton, L.: Tabes and Optic Atrophy, Brit. J. Ophth. **6**:289, 1922.

12. Berger, cited by Igersheimer.[9]

13. Sloan, L. L., and Woods, A. C.: Perimetric Studies in Syphilitic Optic Neuropathies, Arch. Ophth. **20**:201 (Aug.) 1938.

for accurate quantitative decisions. Some ophthalmologists are of the opinion that perimetric studies with small (1 and 3 mm.) white test objects will elicit the presence of very early functional loss, comparable to quantitative studies with colored test objects, and that such a pro-

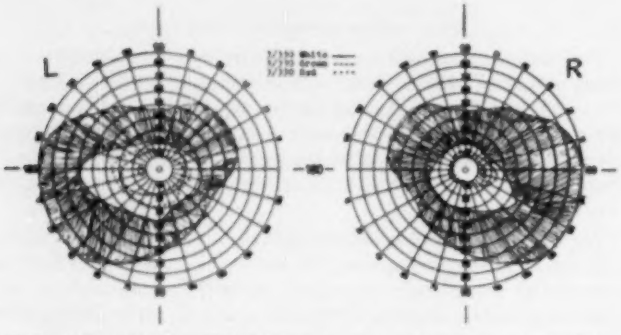


Fig. 1 (case 1).—Visual field defects in the preatrophic stage of optic nerve atrophy, showing contraction for form and color. The disks were normal in color. Vision was 6/6 in each eye.

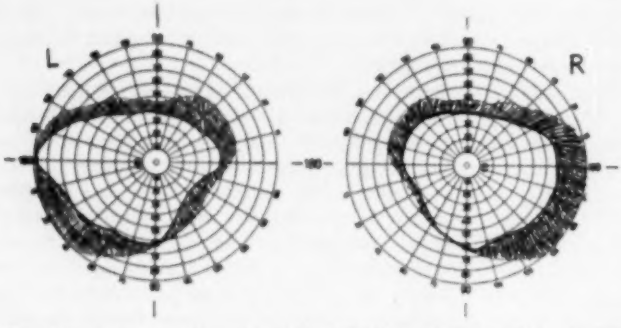


Fig. 2 (case 1).—Improvement of visual fields (to 3/330) in September 1947. In February 1946, 4,200,000 units of penicillin was administered, and in April 1947 induced malaria therapy and 8,000,000 units of penicillin were given. Perimetric fields in March 1948 were normal. Vision was still 6/6.

cedure is more practical, less time consuming and more satisfactory in the examination of clinic patients. That has been our experience.

The Preatrophic Stage.—Patients 1, 2, 3 and 4 (figs. 1 to 5), with neurosyphilis, on repeated examination showed variable degrees of constriction of the visual field for form and color. Central visual acuity

and both optic disks were normal in 2 of the 4 patients; in each of the remaining 2 patients one optic disk was normal in color. After treatment (with penicillin and, in 3 patients, with induced malaria also) the visual field defects disappeared. We did not observe this change after treatment of patients with syphilitic optic nerve atrophy if the optic disks were pathologically pale at the beginning of treatment. A possible exception is the optic disk of the left eye of patient 4. Before treatment, in 1944, the disk was regarded as pale and the right disk as normal. When the patient was again seen, four years later, the appearance of both disks was regarded as within the normal range, although there was a difference in color of the two disks. Either there was an error in evaluation of the color of the left disk on first examination, or restoration of color had occurred when the patient was again seen four years later.

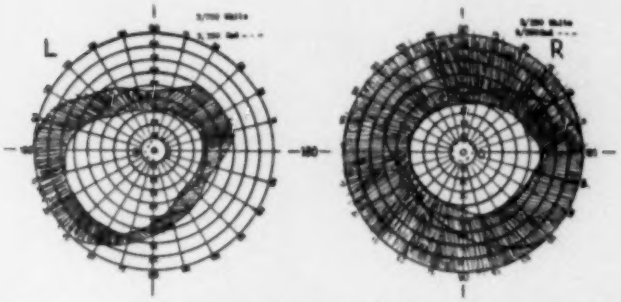


Fig. 3 (case 2).—Concentric contraction of visual fields for form and color in the preatrophic stage of optic nerve atrophy. The optic disks were normal in color. The patient had tabes and was first seen for refraction. Only chemotherapy had been administered. Vision was 6/5 — 2 in each eye with correction.

In accordance with the observations of Bruetsch,[8] the optic nerves of our patients were in the inflammatory, or preatrophic, stage and were amenable to antisyphilitic therapy, in contrast to the atrophic stage, in which the changes are irreversible and the goal of treatment is merely to retard or check the progress of the disease.

Further clinical studies are needed to determine how frequently the field defect occurs as the only evidence of preatrophic change in the optic nerve, the effect of antisyphilitic treatment on the defect and the time required for central visual loss and pallor of the disk to occur in the treated and in the untreated patients. The answers to these questions are doubtless dependent on the intensity and rate of progress of the pathologic process. The location of the lesion, too, will determine the character of the field defect—peripheral or central or mixed.

The inflammatory processes of late syphilis are notoriously slow. The course of optic nerve atrophy (in the atrophic stage) is variable; in some patients blindness ensues in one year or less from the onset of subjective loss of visual acuity. On the other hand, the disease, though untreated, may progress but slowly for years (fig. 7 and case 7). This is also illustrated in the case of another patient, aged 62, with syphilitic primary optic nerve atrophy. With correction, visual acuity was 5/60 in one eye and 6/30 in the other. He had never received antisyphilitic treatment. He had first noticed impaired vision ten years previously and had had diplopia twenty-five years prior to examination. Behr [8] pertinently stated the opinion that the pathologic process of syphilitic optic nerve atrophy exists for a long time prior to disturbance of visual acuity.

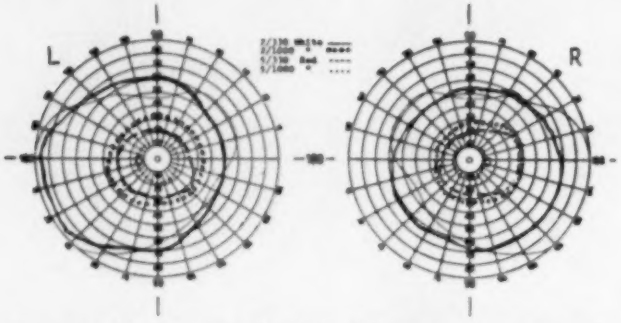


Fig. 4 (case 2).—Normal visual fields in December 1948, after treatment. Penicillin had been administered twice, as well as chemotherapy. Vision was 6/5 in the left eye and 6/5 —2 with correction in the right eye.

Apparently, then, there is an interval in the evolution of optic nerve atrophy, at least in some patients (cases 1, 2, 3 and 4 and the left eye in figure 6), in which the diagnosis can be made in the inflammatory, or preatrophic, stage of the disease. Treatment in this stage obviously affords better prognosis than in the atrophic stage.

It will be observed that in 1 of our patients (case 1) contraction of the visual fields without impairment of central visual acuity or pallor of the disk was observed for three years, although in this interval chemotherapy was administered. It will further be observed that in 2 patients (cases 1 and 2) chemotherapy alone did not cause disappearance of the contraction, nor did the initially employed smaller total dose of penicillin (case 2).

Some authors have stated the opinion that syphilitic optic nerve atrophy may first be evident as pallor of the disk. It is difficult to

conceive of atrophy without loss of function. We have observed frank pallor of the disks in patients with neurosyphilis who had normal, or near normal, visual acuity and normal visual fields. Such an occurrence is apparently rare and would challenge the diagnosis of optic nerve atrophy until loss of function occurred.

In this connection, cases 5 and 6 are pertinent. In case 5 there were third and fourth nerve paralyses of one eye with other clinical signs, as well as serologic evidence, of neurosyphilis. Both disks were pale. Peripheral field and tangent screen studies showed no abnormalities. The patient had normal visual acuity of the right eye, with which he fixed. The left eye was everted and covered by the left lid. Vision was 6/12. This reduction may have been due in part to functional loss incident to disuse, or it may represent an initial functional loss of optic nerve atrophy. In case 6 the temporal side of both optic disks was

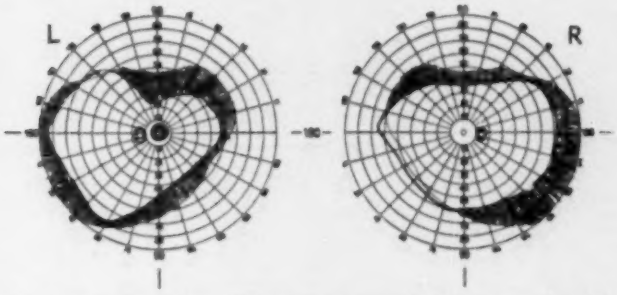


Fig. 5 (case 3).—Visual field defects of early optic nerve atrophy (?) in the left eye and of the preatrophic stage in the right eye. After penicillin and induced malaria therapy, the visual field defects disappeared, and central visual acuity improved in both eyes.

The left eye showed central and pericecal scotomas for 3/330 white and a pale disk on the temporal side. Visual acuity was 2/60, correctible to 3/60. The right eye showed a pericecal scotoma and normal disk with vision of 6/20 + 3, correctible to 6/9.

definitely paler than usual. This may be attributed to a temporal slant exhibited by the disks or to an early atrophic change preceding loss of function. Visual acuity was about normal; peripheral field and tangent screen studies showed no abnormalities. These cases illustrate the difficulty in early diagnosis of optic nerve atrophy.

Igersheimer [14] occasionally observed patients belonging in the aforementioned category. He cited the case of a tabetic patient who, when first seen in 1921, had definite pallor of the disk; visual acuity was 6/12 in the right eye and 6/6 in the left eye. There were no visual field

14. Igersheimer,[9] p. 357.

defects or abnormality in dark adaptation. The author observed no change when he again examined the patient in 1924 and 1925. Igersheimer stated the opinion that in such cases one is forced to the conclusion that pallor of the disk is not a sure sign of atrophy of the nerve tissue.

Bruetsch [15] did not observe any histologic evidence of degeneration of the optic nerve in a patient who had neurosyphilis, with white optic disks but no visual loss or visual field defects.

Kestenbaum [16] and others emphasized loss of capillarity of the optic disks as diagnostic evidence of optic nerve atrophy. In our experience, this symptom occurs too late to have any consideration in early diagnosis of the disease.

Early Atrophic Stage.—We regard pallor of the disk with functional loss as evidence of the atrophic stage of optic nerve atrophy. In contrast

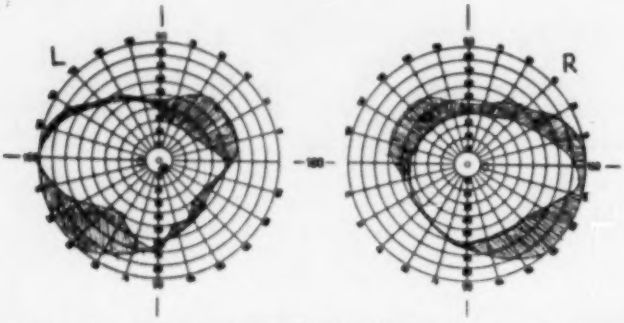


Fig. 6.—Visual field defects (to 3/330 white) of early optic nerve atrophy in the right eye and of the preatrophic stage in the left eye. The patient had tabes and had come to the clinic for refraction.

The left eye showed paracentral scotoma and a normal disk. The blindspot was not enlarged to 10/1,000. Vision was 6/6, correctible to 6/6 + 3. The disk in the right eye was pale.

to cases 1, 2, 3 and 4 and figures 1 to 5, representing the preatrophic stage, figures 6 and 7 and case 7 are presented as illustrating the atrophic stage. Figures 6 and 7 show field defects preceding the complaint of visual loss in patients with tabes who had no knowledge of their disease or of ocular involvement.

The patient represented in figure 6 came to the clinic for refraction; his visual acuity with correction was normal. Visual field defects in both eyes are shown in the figure. It will be noted that the optic disk

15. Bruetsch, W. L.: Personal communication to the authors.

16. Kestenbaum, A.: Clinical Methods of Neuro-Ophthalmologic Examination, New York, Grune & Stratton, Inc., 1946, pp. 56 and 81.

only of the right eye was pale, involvement of the left eye being apparently in the preatrophic stage. This occurrence (and possibly a similar condition in the right eye in case 3, figure 5, and the right eye in case 4) supports the thesis that syphilitic optic nerve atrophy occurs in what appears to be the preatrophic stage with normal color of the disk and with normal central visual acuity.

The patient represented in figure 7 visited the clinic for treatment of conjunctivitis. He was not aware of visual loss in both eyes. There was pallor of the disks only on the temporal side. The visual field defects are shown in the figure. Two years later, during which the patient neglected to have treatment, the entire disks were pale.

Patient 7 visited the clinic because of diplopia. Extraocular movements were full. Corrected visual acuity was normal. There was pallor of the disks only on the temporal side. He lapsed in attendance

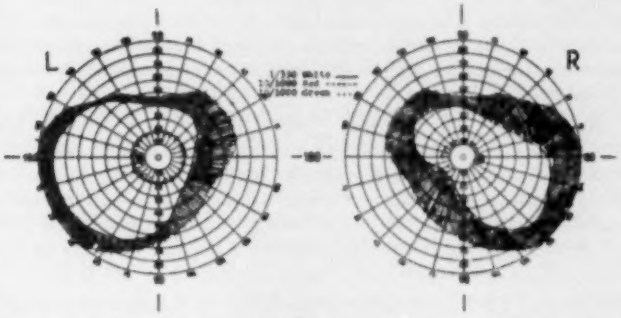


Fig. 7.—Visual field defects of early optic atrophy in a patient with tabes who came to the clinic because of conjunctivitis. Visual acuity was 6/12 in each eye. When he was first seen, both disks were pale on the temporal side only. No central scotomas were seen with the white 2 and 3 mm. test objects. Two years later (antisyphilitic treatment had been neglected) the entire disks were pale; central visual acuity was further reduced in the left eye (to 6/9) and the visual field defects remained unchanged.

at the clinic for thirty-one months, at the end of which time the entire disks were pale, with considerable loss of visual acuity.

These cases are evidence that early in the course of optic nerve atrophy pallor of the disk may be confined to the temporal side.

COMMENT

If only in emphasis of the possibility of early diagnosis of syphilitic primary optic nerve atrophy by a peripheral field defect as an initial and only symptom, the disease should be envisaged and taught as a two stage process.

It requires no clinical acumen to diagnose optic nerve atrophy in a patient with neurosyphilis who has pale optic disks and visual field defects. So far as a rapid course to blindness is concerned, a diagnosis at this stage is somewhat comparable to the diagnosis of malignant disease from cachexia.

It should be emphasized that in 4 of 5 cases recorded here (cases 1 and 2 and the cases represented in figures 6 and 7) the only motivation for perimetric study was the principle that for every patient with neurosyphilis such a study is indicated. Only in this way can optic nerve atrophy be diagnosed early and opportunity afforded to combat syphilis as a cause of blindness.[17]

To facilitate the early diagnosis of optic nerve atrophy, it is necessary that ophthalmologists and all physicians who examine patients with syphilis have a high degree of awareness of the optic nerve and "reach out" for the diagnosis in the preatrophic stage of impending optic nerve atrophy or in the early stage of atrophy (figs. 6 and 7 and case 7), before the patient is aware of visual loss. In the records of private, ward and clinic patients, too infrequently is no mention made of such examination unless the patient complains of visual loss or tryparsamide therapy is given.[18]

In order that the diagnosis of optic nerve atrophy may be made early, ophthalmologic and perimetric examinations should be made on all patients with neurosyphilis whether the serologic reactions of the blood and spinal fluid are positive or negative. Any physician can detect pupillary abnormalities. If they are found, examinations of the spinal fluid should be made to exclude optic nerve atrophy. Failure to make ophthalmologic examination of a syphilitic patient in the late stage of infection without evidence of neurosyphilis would not, in our opinion, constitute an important error of omission.

The ophthalmologist is well situated to exclude optic nerve atrophy of every patient examined with pupillary abnormalities. The industrial physician is likewise in a favorable position to expedite the diagnosis of early syphilitic optic atrophy, since he encounters in mass examinations the type of person who is likely to have the disease, one whose infection is unknown to himself and remains untreated.

Facilities should be made for routine ophthalmologic examination of selected patients in clinics treating syphilis.

It should be emphasized that treatment in the preatrophic stage in the cases reported prevented progress of the disease and preservation of visual acuity. The problem of syphilitic optic nerve atrophy in causing

17. Further discussion of the 10 to 15 per cent of blindness caused by syphilis is afforded in our previous communication.[1]

18. This statement is based on a review of case records of patients with neurosyphilis in a general hospital.

blindness does not concern entirely a lack of therapeutic response in the atrophic stage but, rather, is related to early diagnosis. It is far better for the patient that his syphilitic infection be evaluated in relation to early stages of the devastating forms of the disease—cardiovascular syphilis, neurosyphilis and optic nerve atrophy—rather than in terms of positive or negative serologic reactions. The ophthalmoscope and perimeter are as essential as the spinal puncture needle in the diagnosis and management of syphilis and its complication, primary optic nerve atrophy.

REPORT OF CASES

CASE 1.—*Preatrophic stage of optic nerve involvement.*

N. S., a white girl aged 13, was first seen in December 1943. She was referred for ophthalmologic examination by a venereal disease clinic (Department of Public Health, Philadelphia) as having juvenile tabes. She had received five injections of an arsenical and fourteen injections of a bismuth compound.

Both pupils were irregular, semidilated, stiff to light but reactive in accommodation. The biceps and triceps reflexes were hypoactive; the patellar and achilles reflexes were absent. There were no symptoms suggestive of dementia paralytica. Visual acuity was 6/6-2 in the right eye and 6/6-3 in the left eye. The optic disks were normal in color and their margins well defined; there were no pathologic lesions in the fundi. The perimetric fields, showing marked contraction for form and for color, are seen in figure 1. The serologic tests for syphilis were strongly positive; the spinal fluid gave positive reactions in all phases, and the colloidal gold curve was 0012234320.

Treatment, given from December 1943 to February 1946, consisted of twenty-four injections of an arsenical and thirty injections of a bismuth compound. Repeated perimetric field studies showed persistent contraction. The sodium salt of penicillin was administered in February 1946, and injections were given every three hours for seven and a half days, for a total dose of 4,200,000 units. Chemotherapy was discontinued.

Early in 1946 symptoms suggestive of dementia paralytica appeared; the patient became difficult to manage at home and in school; she was uncooperative, at times sulky, independent, flippant and self willed. She showed impairment of attention and concentration, but was oriented and had no symptoms of psychosis. Neurologic signs remained unchanged except for some slurring of speech. The colloidal gold curve was then of the dementia paralytica type. In April 1947, malaria therapy was instituted (one hundred and eleven hours of fever at a temperature of over 100 F.), and 8,000,000 units of penicillin was given. Subsequent to this therapy symptoms of dementia paralytica gradually disappeared, and no further treatment was given. The perimetric field of September 1947 showed considerably less contraction (fig. 2). Examination of the spinal fluid in May 1948 revealed no abnormality except for a positive Wassermann reaction in the first two dilutions only. Perimetric examination in March 1948 and March 1949 showed normal fields. The optic disks remained normal in color. Central visual acuity has not changed since her first admission.

CASE 2.—*Preatrophic stage of optic nerve involvement.*

G. F., a white woman aged 51, was first seen in May 1946.[19] Because of a positive Wassermann reaction, she had received injections in the arms and

19. This case is case 6 in our previous communication.[1]

buttocks at irregular intervals for "many years." She desired a change in her glasses; other than the visual impairment, and occasional lancinating pains in the legs of several years' duration, she had no complaint.

She presented the neurologic abnormalities of tabes. Both optic nerves were normal in color. Visual acuity in the right eye was 6/22 without correction and 6/5-2 with correction; in the left eye it was 6/22 without correction and 6/5-2 with correction. The perimetric fields showed concentric contraction to form and color, as portrayed in figure 3. Repeated examinations showed the same degree of contraction. The Wassermann and Kahn reactions were positive. Serologic tests on the spinal fluid gave negative reactions in all phases. We were informed by the physician who treated her that therapy consisted of injections of arsenical and bismuth compounds; no tryparsamide had been administered. About one year previously a physician had administered penicillin, about 100,000 units being given three times in one week and then weekly for six weeks.

In December 1946 the sodium salt of penicillin was administered every three hours for a total dose of 6,400,000 units, given in seven and one-half days. She was not seen again until December 1948. She had gained in weight and had no complaint except for pains in the legs, which were less pronounced. She had been treated by several physicians. She had had daily injections of 300,000 units of penicillin in oil for fourteen consecutive days and "many" injections of a bismuth compound. Her visual acuity with correction was the same as on first examination; the optic disks were normal in color, and the perimetric fields were normal (fig. 4). The serologic reactions for syphilis were less positive than on her first admission.

CASE 3.—*Preatrophic stage of optic nerve involvement.*

A. S., a white woman aged 52, was first seen in December 1947. Her chief complaint was impaired vision of the left eye, of eight months' duration, appearing after a "nervous breakdown." At that time she had crying spells and impaired memory and was at times confused. For the past ten years she had had occasional sharp pains in both legs.

Station and gait were normal; motor power and coordination were good, and sensation was intact over the trunk and extremities. The patellar reflexes were hyperactive and unequal on the two sides; achilles reflex was absent on the right and diminished on the left. There were pupillary abnormalities. The serologic reactions for syphilis were strongly positive; the spinal fluid gave a positive reaction only in some phases. Visual acuity was 6/20 + 3 in the right eye without correction and 6/9 with correction; in the left eye it was 2/60 without correction and 3/60 with correction. The right optic disk was normal; the left showed questionable pallor on the temporal side. The peripheral fields are shown in figure 5. Tangent screen tests showed a normal central field in the right eye except for a relative pericecal scotoma to 2/1,000 white, and in the left eye contraction of the upper field, a relative pericecal scotoma to 2/1,000 white and a central scotoma to 2/1,000.

In January 1948 the patient was given induced malaria therapy and, at the same time, 6,000,000 units of penicillin G administered in eight days. After this therapy there was gradual disappearance of her "nervous" symptoms; she gained weight, and her emotional tone became normal. Repeated perimetric fields showed gradual disappearance of the constriction and gradual improvement of visual acuity in the left eye. In March 1949 the peripheral fields were full; with correction visual acuity was 6/15 in the left eye and 6/9 in the right eye. Tangent screen studies in July 1949 showed absence of scotomas. Visual acuity in the left

eye was 6/30, correctible to 6/15; in the right eye it was 6/21, correctible to 6/6. There was still questionable pallor of the temporal side of the left disk.

CASE 4.—*Preatrophic stage of optic nerve involvement.*

S. J., a white man aged 35, was first seen in March 1944. He was referred for ocular examination because tryparsamide was considered in treatment of his neurosyphilis. He had had a chancre in 1929, for which metal chemotherapy was given at irregular intervals until 1938. He had received no further treatment until 1944, when thirty injections of a bismuth compound were given. His only complaint was stabbing pains in both legs, occurring at irregular intervals. He presented neurologic signs of tabes. The serologic reactions for syphilis were positive, and the spinal fluid gave a positive reaction in all phases.

Visual acuity with correction was 6/6 in the right eye and 6/15 in the left eye. Details of the right optic disk were obscured by prepapillary veiling; the color was definitely pale. The perimetric fields showed a slight to moderate concentric contraction above, chiefly of 10 to 20 degrees in each eye. These changes were confirmed. There was no central scotoma or enlargement of the blindspot.

In September 1944 the sodium salt of penicillin was given every three hours for a total dose of 3,200,000 units in eight days; at the same time induced malaria treatments were given. He had one hundred and twenty-five hours of fever with temperatures over 100 F. and eighty-nine hours with temperatures over 102 F. He lapsed from further observation until October 1949. At this time he had no subjective complaint except for the stabbing pains in the legs; these, however, were less severe and occurred at longer intervals.

Visual acuity in each eye was the same as in March 1944. The optic disks showed a degree of coloration which could be said to be within normal, although there was a slight difference in color of the two disks. The perimetric fields of both eyes were full.

CASE 5.—*Pallor of optic disks without loss of function.*

S. M., a white man aged 38, was first seen in June 1948. At the age of 18 he had a genital lesion, for which he received only local treatment. Nine years prior to admission he had diplopia, ptosis of the left eyelid and turning out of the left eye. These symptoms remained unchanged. At their onset he received about two years' treatment with injections, most of which were given in the buttocks.

He was first seen by an ophthalmologist (now deceased) in December 1939. We were informed that the record cited the following findings: Corrected visual acuity was 20/20 in both eyes. There were pupillary abnormalities, and the Wassermann reaction of the blood was strongly positive. The record made no mention of examinations of the fundi or of ocular muscle balance. Another ophthalmologist examined the patient in January 1940. He informed us that, according to his record, "the oculomotor nerve was involved and all muscles supplied by the third nerve were paralyzed." His record made no mention of the fundi or of perimetric studies.

Six months prior to admission the patient received daily injections of depot penicillin G for twenty-three days, for a total dose of 12,000,000 units. No improvement of ocular symptoms followed this treatment.

On his admission corrected visual acuity was 6/6-1 in the right eye and 6/12-2 in the left eye. The right disk was somewhat pale; the left showed definite gray pallor of the entire disk. The fundi appeared otherwise normal. The peripheral fields for form and color were normal, and tangent screen studies showed no

abnormalities; the blindspot of the left eye, however, could not be outlined satisfactorily. This was attributed to inability of fixation. Both pupils were dilated and irregular and did not react to light or in accommodation. There was partial paralysis of the third and fourth nerves with involvement of the extraocular muscles and the levator palpebrae, causing outward and downward rotation of the left eye and ptosis. The ptosis apparently later became functional in an attempt to avoid diplopia, since when he elevated the lid diplopia occurred. The only other neurologic abnormalities were absence of the right achilles reflex; the left was obtained only on reenforcement. The roentgenogram showed no evidence of disease in the skull, the sella turcica, the orbits or the paranasal sinuses. Serologic tests for syphilis gave positive reactions. Examination of the spinal fluid revealed 8 lymphocytes per hundred cubic centimeters, a faint trace of globulin, a colloidal gold curve of 0002332000, a Wassermann reaction of 444, and a total protein of 130 mg. per hundred cubic centimeters.

CASE 6.—*Pallor of optic disks without loss of function.*

W. C., a Negro aged 51, was first seen in April 1949, with the complaint that his "eyes ran water and hurt." He had mild conjunctivitis of both eyes. He had had a genital lesion in 1929, for which he received antisyphilitic treatment for several months and subsequently at irregular intervals.

Visual acuity was 6/9 in each eye, correctible to 6/6 in the left eye. There was a temporal slant of both optic disks, and the color on their temporal sides was paler than normal. Peripheral field and tangent screen studies of both eyes showed no abnormalities. The patient presented pupillary and other neurologic abnormalities suggestive of tabes and had occasional cramplike pains in both legs. Serologic tests for syphilis gave negative results, and the reaction of the spinal fluid was negative in all phases. (These negative results could have resulted from antisyphilitic treatment he had received.)

CASE 7.—*Early atrophic stage of optic nerve involvement.*

P. S., a Negro aged 35, was first seen in August 1944, with the complaint of double vision when looking to the left. Visual acuity in the right eye was 6/9, correctible to 6/6; that in the left eye was 6/12, correctible to 6/6. Extraocular movements were full. The temporal halves of both optic disks were pathologically pale. He lapsed from attendance at the clinic before complete study was made.

He returned in March 1947. Diplopia had disappeared (a reason for his not returning in 1944). He now complained of impaired vision of six months' duration. He had had inadequate antisyphilitic treatment several years prior to 1944. Visual acuity in the right eye was 6/60 with and without correction; vision in the left eye was 6/15, correctible to 6/12. Both optic disks were pale. The peripheral field of the right eye showed concentric contraction of 20 to 30 degrees to the 3 mm. white test object, a relative central scotoma to the 2 mm. white test object and a relatively normal blindspot. The peripheral field of the left eye showed a slight superonasal contraction to the 3 mm. white test object. The tangent screen test showed normal central fields.

He had neurologic abnormalities of the tabetic type of neurosyphilis. The Wassermann reaction of the blood was strongly positive; the spinal fluid gave positive reactions in all phases.

1934 Spruce Street, Philadelphia (Dr. Klauder).

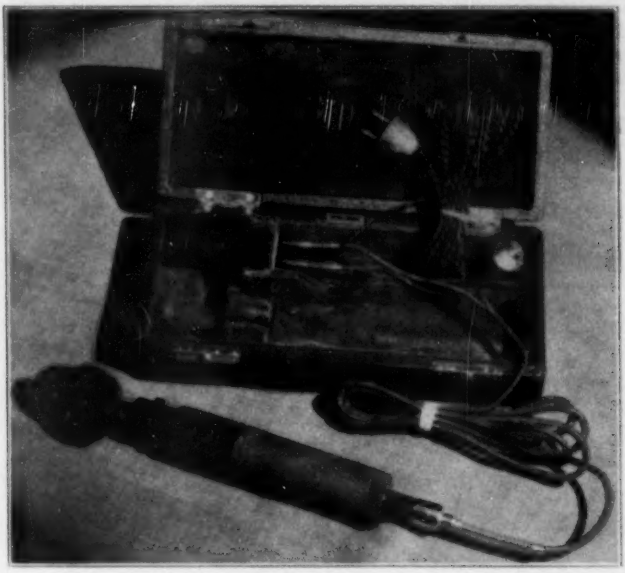
410 Haddon Avenue, Camden, N. J. (Dr. Meyer).

Clinical Notes

TRANSFORMER FOR THE A O "GIANTSCOPE"

JOHN L. GOFF, M.D.
BOSTON

In order to facilitate the portability of the A O "giantscope," the following arrangement has been found satisfactory. A transformer, providing 6.3 volts and 1.2 amperes, which is small enough to fit into the original box is installed. This is connected with alternating current by



Transformer for the American Optical Company "giantscope."

means of an extension cord. The "giantscope" with its cord is connected to the transformer by means of two plugs. This arrangement works well with alternating current. A satisfactory resistor with respect to size has not as yet been devised for use with direct current.

243 Charles Street.

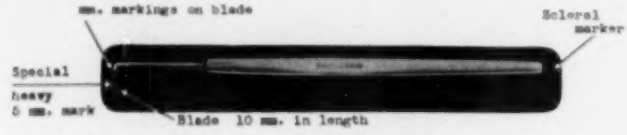
From the Home Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

MUSCLE HOOK

DAVID E. ROLF, M.D.
CLEVELAND

This muscle hook is made of stainless steel and has a thin, flat blade, which is 10 mm. long. It has small, fine millimeter markings, with a special heavy marking at the 5 mm. point. The blade is designed at right angles to the handle; and the tip of the handle has a sharp, small scleral marker, which can be used in muscle surgery as a marking device.

The instrument has the following features: 1. The thin, narrow blade permits ease in manipulation. 2. Millimeter markings aid in



Muscle hook. The blade is flattened and thinned for ease of manipulation.

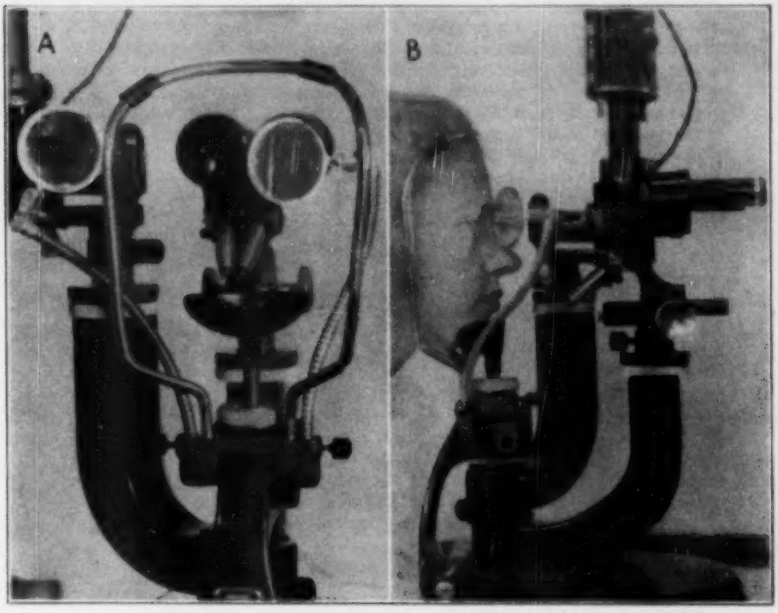
quick estimation of the width and thickness of the muscle and in rapid appraisal of the various measurements which are used in ocular surgery, especially muscle surgery. 3. The scleral marker at the tip eliminates the need for an extra instrument and facilitates the operative procedure. 4. The blade is long enough to allow the tendon of the muscle to be gently stretched over the surface. This helps immeasurably during the process of suturing.

This instrument may be obtained from V. Mueller & Co., Chicago. 1017 Republic Bldg. (15).

A FIXATION AID FOR SLIT LAMP BIOMICROSCOPY

DAVID D. DONALDSON, M.D.
AND
DAVID G. COGAN, M.D.
BOSTON

In the course of an examination with the slit lamp, an attempt is usually made to keep the subject's eyes stationary, and yet directed straight ahead, by having him fixate on the examiner's forehead or on



A, front view of the slit lamp biomicroscope with the right fixation aid in place for use during examination of the left eye. *B*, side view, with the fixation aid placed before the subject's right eye and the slit lamp biomicroscope adjusted for examination of the left eye.

some part of the microscope. While probably satisfactory for all practical purposes, the procedure has several disadvantages: The observer's head and, to a less extent, the microscope are not themselves stationary; they are not visible when the examination is done in a dark room, and they are so close to the subject that fixation is tiring for the presbyopic or prepresbyopic patient.

From the Howe Laboratory of Ophthalmology, Harvard Medical School.

To overcome these difficulties and to permit a ready variation in fixation, we have found the following procedure satisfactory for all but one-eyed patients. Two mirrors about 5 cm. in diameter are attached to the chin rest base by means of a flexible cable [1] in such a way that each mirror may be placed in front of one eye (figure, *A* and *B*). Since the mirrors are attached to the cables by means of ball and socket joints, they may be rotated through any angle and will maintain any position in which they are placed. At the same time, either or both mirrors may be deflected out of the way when not in use.

When one eye is to be examined, the mirror is placed before the other eye. It is turned at a convenient angle so that some luminous object in the room may be fixated. Variation of fixation may then be accomplished by simple rotation of the mirror. As an added variant that is convenient, but not always necessary except when examination is done in complete darkness, we have used for the fixation object a spot of light projected on the wall, and this, too, may be varied at will.

This method of facilitating fixation is simple and useful for all biomicroscopy of the eyes, but it is especially indicated when accurate, prolonged and yet variable fixation is desired. We have found it of particular value for such purposes as removal of foreign bodies under slit lamp control, for special studies such as measurements of corneal thickness and for demonstrations of lesions in which change of examiners vitiates the usual methods of fixation.

243 Charles Street.

1. Bronze flexible hose (outside diameter, 5/16 inch), obtained from A. E. Borden Co., 142 High Street, Boston 10.

News and Notes

EDITED BY DR. W. L. BENEDICT

ANISEIKONIA PATENTS DEDICATED

The United States Patent Office has announced that the Hanover Institute, Hanover, N. H., does "assign, transfer, give, and dedicate the following Letters Patent and the inventions therein specifically claimed to the people of the United States of America for public use forever." The twenty-six patents listed were granted while the Dartmouth Eye Institute was interested mainly in problems of binocular vision, especially aniseikonia.

Copies of the patents may be obtained from the United States Patent Office, Washington 25, D. C., at 25 cents each.

SOCIETY NEWS

Nineteenth Annual Spring Clinical Conference of the Southern Clinical Society.—The Nineteenth Annual Spring Clinical Conference of the Southern Clinical Society will be held March 13 to 16, 1950, at Hotel Adolphus and the Baker Hotel, Dallas, Texas. The registration fee of $20 will admit one to all features of the conference, including lectures, luncheons, evening meetings and the annual banquet on Thursday evening.

The guest speaker for the section in ophthalmology will be Dr. John M. McLean, New York, who will discuss "Ophthalmological Approach to Progressive Postoperative Exophthalmos," "Use of Anticoagulants in Ophthalmology," "Present Status of Corneal Transplantation" and "Modern Surgery of Oblique Muscles."

Dr. Robert E. Votaw, St. Louis, will be guest speaker for the section on otolaryngology. He will discuss "Sinusitis and Chronic Pulmonary Disease." "Headache from the Otolaryngologist's Viewpoint," "Sinusitis in Children" and "Recent Advances in Surgical Treatment of Malignant Growths of the Pharynx and Larynx."

At a clinic meeting on Wednesday afternoon, March 15, a discussion of recent therapeutic advances in ophthalmology and otolaryngology will be led by Dr. Andres Goth. The program includes "Antibiotics," Dr. Goth; "Antihistamines," Dr. Arthur Grollman; "New Miotics in Glaucoma," Dr. Lester H. Quinn; "Management of Acute Rhinosinusitis," Dr. J. Dudley Singleton; "Cataract Extraction for the Occasional Operator," Dr. Maxwell Thomas, and "Diagnosis of Vertigo," Dr. Lyle M. Sellers.

GENERAL NEWS

Postgraduate Conference in Clinical Ophthalmology.—The Stanford University School of Medicine will present a postgraduate conference in clinical ophthalmology from March 27 to 31, 1950. Registration will be open to physicians who limit their practice to the treatment of diseases of the eye or the eye, ear, nose and throat. Instruc-

tors will be Dr. A. Edward Maumenee, Dr. Dohrmann K. Pischel, Dr. Jerome W. Bettman, Dr. Earl H. McBain and Dr. Arthur J. Jampolsky.

In order to allow free discussion by members of the conference, registration will be limited to 30 physicians. Programs and further information may be obtained from the office of the dean, Stanford University School of Medicine, 2398 Sacramento Street, San Francisco 15.

Annual Spring Convention in Ophthalmology and Otolaryngology, University of Oregon.—The Annual Spring Convention in Ophthalmology and Otolaryngology will be held in Portland, Ore., March 19 to 24, 1950. A fine program has been arranged by the Oregon Academy of Ophthalmology and Oto-Laryngology and the University of Oregon Medical School. This year the meeting has been divided into two sections: (1) otolaryngology, which will be held on Monday and Tuesday and on Wednesday morning, and (2) ophthalmology, which will be held on Wednesday afternoon, Thursday, and Friday morning. Guest speakers are Dr. John R. Lindsay, professor of otolaryngology at the University of Chicago School of Medicine; Dr. Gordon D. Hoople, professor of otolaryngology at the Syracuse University College of Medicine; Dr. Paul Chandler, professor of ophthalmology at Harvard Medical School, and Dr. Michael Hogan, associate professor of ophthalmology at the University of California Medical School.

On Thursday evening, March 23, Dr. Chandler will deliver the first John E. Weeks Memorial Lecture in Ophthalmology. Friday afternoon and evening, March 24, the Pacific Coast Section of the Association for Research in Ophthalmology, Inc., will hold its annual meeting.

Postgraduate Conference in Ophthalmology, University of Michigan Medical School.—The department of postgraduate medicine of the University of Michigan Medical School announces the annual conference in ophthalmology for qualified physicians, April 24 to 26, 1950, to be given at the Horace H. Rackham Graduate School Building, Ann Arbor, under the direction of the department of ophthalmology. Guest lecturers are Dr. John B. Hitz, Milwaukee; Dr. Herman Elwyn, New York; Dr. Albert E. Sloane, Boston; Dr. Paul L. Cusick, Detroit, and Dr. Kenneth C. Swan, Portland, Ore. Resident lecturers are: Dr. F. Bruce Fralick, Dr. Harold F. Falls and Dr. John W. Henderson.

The complete program and details will be mailed on request addressed to Dr. Howard H. Cummings, Chairman, Department of Postgraduate Medicine, University Hospital, Ann Arbor, Mich.

Training Course for Orthoptic Technicians.—The American Orthoptic Council is announcing the third annual training course for orthoptic technicians. This course was previously given in Maine in 1948 and in Boston in 1949. The current course will begin in Boston on July 5, 1950. The didactic portion of the course will last through August 30, the tuition fee being $150 and room and board $100. The practical portion of the course will be given in various teaching clinics and offices throughout the country during the succeeding year. Nationally known ophthalmologists and certified orthoptic technicians will aid

Dr. Walter B. Lancaster with the didactic instructions. Scholarships for worthy students may be available. Further information concerning the course may be obtained from the office of the American Orthoptic Council, 1605 Twenty-Second Street, N. W., Washington 8, D. C. The dead line for receiving applications is July 1, 1950.

Establishment of Eye Bank, Grady Memorial Hospital, Atlanta, Ga.—The Clay Memorial Eye Clinic and the Emory University School of Medicine, through the William L. Crawley Fund, have established an eye bank at the Grady Memorial Hospital, 36 Butler Street, S. E., Atlanta 3, Ga. The facilities of the eye bank are available, without charge, to ophthalmologists and cooperating hospitals throughout the Southeast and any other region of the country. Local transportation for the Atlanta area is provided by the Atlanta chapter of the American Red Cross Motor Corps, and regional transportation is provided through the Capital, Delta, Eastern and Southern airlines. Those airlines have offered their facilities without cost. Any information regarding the function of the eye bank may be obtained from the Eye Bank, Clay Memorial Eye Clinic, 72 Armstrong Street, S. E., Atlanta 3, Ga.

Certification by the American Board of Ophthalmology.—Candidates for certification by the American Board of Ophthalmology are accepted for examination on the evidence of a written qualifying test. These tests are held annually in various parts of the United States.

Applications are now being accepted for the 1951 written test. They will be considered in order of receipt until the quota is filled. Practical examinations for acceptable candidates will be held on the following dates: May 22-26, 1950, Boston; October 2-6, 1950, Chicago; January 1951, West Coast.

A new directory of all certified specialists to date, arranged alphabetically and geographically, will be published early in 1950. No biographic material is included. Certified specialists are urged to keep the Board office informed of all changes of address.

Continuation Course in Ophthalmology, Tulane University of Louisiana.—A continuation course in ophthalmology will be given in New Orleans, March 13 to 18, 1950, by the department of ophthalmology of Tulane University of Louisiana School of Medicine and the Division of Graduate Medicine. Guest lecturers will be Dr. Daniel B. Kirby, professor emeritus of ophthalmology, New York University School of Medicine, New York; Dr. Frank B. Walsh, associate professor of ophthalmology, John Hopkins University School of Medicine and Wilmer Ophthalmological Institute, Baltimore; Dr. Robert J. Masters, professor of ophthalmology, Indiana University School of Medicine, Indianapolis; Dr. Harold F. Falls, associate professor of ophthalmology, University of Michigan Medical School, Ann Arbor, Mich.; and Dr. Charles Sheard, distinguished lecturer in ophthalmology, Tulane University of Louisiana School of Medicine, and professor emeritus of experimental biophysics, Graduate School, University of Minnesota (Mayo Foundation). Additional lectures will be given by resident faculty members of the department of ophthalmology, Tulane University.

The Americas United to Save Sight.—A midcentury conference on progress will be held on March 26 to 31, 1950, under the joint auspices of the National Society for the Prevention of Blindness (annual meeting) and the Pan-American Association of Ophthalmology (interim session), at the Floridian Hotel, Miami Beach, Fla. The program follows:

Sunday, March 26

1:00 p.m.: Registration and Viewing of Exhibits

5:00 p.m.: Reception

Evening: Free

Monday, March 27

8:00 a.m.: Registration

9:00-12 Noon: General Assembly

Presiding: Conrad Berens, president, Pan-American Association of Ophthalmology

Mr. Mason H. Bigelow, president, National Society for the Prevention of Blindness

Dr. A. Vazquez Barrière, president, Second Pan-American Congress, Montevideo, Uruguay

Dr. Thomas R. Yanes, president, Third Pan-American Congress, Habana, Cuba

Dr. Antonio Torres Estrada, president, Fourth Pan-American Congress, México, D. F., Mexico

Dr. Cesar Andrade, president, National Council of Education, Rio de Janeiro, Brazil

Welcome by the mayor of Miami Beach, Honorable Harold Turk

Intervention of the State in the Battle Against Blindness

Dr. A. Vazquez Barrière, chairman, Committee on the Prevention of Blindness of the Pan-American Association of Ophthalmology

Testing Visual Fields by Flicker Fusion

Dr. Paul W. Miles, St. Louis

Rice Diet for Hypertension: Fundus Photographic Demonstration

Dr. W. B. Anderson and Dr. Walter Kempner, Duke University, Durham, N. C.

Discussant: Dr. Federico Cerboni, Buenos Aires, Argentina

12:00 Noon: Buffet luncheon in hotel garden

2:00 p.m.: Presiding officers: Dr. A. Vazquez Barrière Montevideo, Uruguay; Dr. John A. MacMillan, Montreal, Canada; Dr. Nelson M. Black, Miami, Fla.

Recent Advances in Ocular Therapeutics

Dr. P. Robb McDonald, Philadelphia

Discussants: Dr. Paulina Satanowski, Buenos Aires, Argentina; Dr. John Bellows, Chicago

New Opportunities in Teaching Ophthalmology

Committee on Teaching of Ophthalmology
Dr. Cecil S. O'Brien, Iowa City
Dr. James H. Allen, Iowa City
Dr. Alberto Urretz Zavalia, Cordoba, Argentina

Preventing Blindness in the Americas

Five minute "Prevention of Blindness" reports from each of the American Republics

Legislation Regarding the Prevention of Blindness

Hermino de Moraes Brito Conde, M.D., Rio de Janeiro, Brazil

8:00 p.m.: Business meeting of the Pan-American Association of Ophthalmology

8:30 p.m.: Preview of Mexico—1952: Color Movies
Dr. Luis Sanchez Bulnes, México, D. F., Mexico

Intraocular Tumors (color photographic demonstration)

Mrs. H. Eleanor Campbell Wilder, Army Institute of Pathology, Washington, D. C.

Tuesday, March 28

9:00 a.m.: Presiding officers: Dr. Bascom H. Palmer, Miami, Fla.; Dr. César de Andrade, Rio de Janeiro, Brazil

Effects of Excessive Sunlight on the Eyes

(*a*) At High Altitudes
Dr. Jorge Valdeavellano, Lima, Peru

(*b*) At Sea Level
Dr. Robison D. Harley and Dr. Robert Peckham, Atlantic City, N. J.

(*c*) Visual Effect of Supersonic Speed
Col. Victor Byrnes, Randolph Field, Texas

Discussants: Dr. John L. Matthews, San Antonio, Texas; Dr. Brittain F. Payne, New York

How Good Are Contact Lenses?

Dr. Baudilio Courtis, chairman, Contact Lens Committee, Buenos Aires, Argentina

Discussants: Dr. Arno Town, New York; Dr. Daniel Silva, Mexico, D. F., Mexico

SYMPOSIUM

Parasitic Diseases

Moderator: Dr. M. Puig Solanes, México, D. F., Mexico, Dr. Rafael Pacheco Luna, Guatemala City; Dr. Nicolino Robello Machado, Santos, Brazil; Dr. Alson E. Braley, New York

Hemispheric Control of Ocular Infections

Dr. Fred L. Soper, director for Western Hemisphere, World Health Organization, Pan-American Sanitary Bureau, Washington, D. C.

Nonpenetrating Keratoplasty

Dr. Jorge Malbrán, Buenos Aires, Argentina

Discussant: Dr. Ramon Castroviejo, New York

12:00 Noon: Luncheon meeting

Chairmen: Dr. Henri Pichette, Quebec, Canada; Dr. Sherman B. Forbes, Tampa, Fla.

2:00 p.m.: Presiding officers: Dr. Franklin M. Foote, executive director, National Society for the Prevention of Blindness; Dr. Luis Sanchez Bulnes, director, Mexican Society for the Prevention of Blindness

Teamwork for Prevention (Panel Discussion)

Discussants:

Frank Woods, president, Illinois Society for the Prevention of Blindness, Chicago

Judge Ned H. Smith, president, Detroit Society for the Prevention of Blindness

Harry Simmons, executive director, Florida Council for the Blind, Tampa, Fla.

Miss Anne E. Geddes, chief, Statistics and Analysis Division, Federal Security Agency, Washington, D. C.

John L. Fortson, director of public relations National Society for the Prevention of Blindness

8:00 p.m.: Evening entertainment on the terrace, arranged by local committee: Drs. Palmer, Richardson, Sayad and Forbes

Wednesday, March 29

9:00 a.m.: Presiding officers: Dr. R. Bellido-Tagle, Lima, Peru; Dr. W. Y. Sayad, West Palm Beach, Fla.

Research in Testing Children's Vision

Dr. Richard G. Scobee, St. Louis

(Title to be supplied)

Dr. Arnold Gesell

Room A: Presiding officer: Dr. Ricardo Fernandez, San Juan, Puerto Rico

ROUND TABLE DISCUSSION ON INDUSTRIAL EYE PROBLEMS

Dr. Albert C. Ruedemann, Detroit

Dr. Lino Vergara Espino, México, D. F., Mexico

Safety director, Florida Light & Power Co.

Personnel director, Florida Light & Power Co.

John Scott Jr., Rocky Mount Hills, Rocky Mount, N. C.

Room B: Presiding officer: Dr. Shaler Richardson, Jacksonville, Fla.

SYMPOSIUM ON TRACHOMA

Trachoma Control in Argentina

Dr. Magin A. Diez, Buenos Aires, Argentina
Dr. Esteban Adrogue, Buenos Aires, Argentina
Dr. Virgilio C. Victoria, Tucuman, Argentina

Trachoma Control in the United States

Dr. A. A. Siniscal, Rolla, Mo.
Dr. K. W. Cosgrove, Little Rock, Ark.

Trachoma Control in Brazil

Dr. Cesario de Andrade, Rio de Janeiro, Brazil

Progress in Treatment of Trachoma in Past Ten Years

Dr. Penido Burnier, Campinas, Brazil

12:00 Noon: Luncheon meeting
Presiding: Dr. Horacio Ferrer, Habana, Cuba

Plans for the 1952 Congress in México, D. F., Mexico

Dr. Antonio Torres Estrada

2:00 p.m.: Presiding officers: Dr. Jorge Balza, Buenos Aires; Dr. Daniel B. Kirby, New York

Recent Advances in Military Ophthalmology

Dr. César A. Rodriguez, Lima, Peru
Col. Victor Byrnes, United States Air Forces
Dr. Feliciano Palomino Dena, México, D. F., Mexico

Visual Acuity Standards for:

Military Forces
Dr. Brittain Payne, New York

Civil Service Personnel
Dr. Blackwell

SYMPOSIUM

Blindness in Premature Babies from Retrolental Fibroplasia

Moderator: Dr. Algernon B. Reese, New York
Dr. Parker Heath, Boston
Dr. Arlington C. Krause, Chicago
Dr. Arthur C. Unsworth, Hartford, Conn.
Dr. William Turnbull, Montreal, Canada

Eye Diseases in Infancy

Dr. Enrique Cipriani, Lima, Peru
Discussion by Dr. John A. MacMillan, Montreal, Canada

7:00 p.m.: Barbecue dinner, buffet style
Presiding officer: Mr. Mason H. Bigelow, New York, president, National Society for the Prevention of Blindness
Welcome: Honorable Fuller Warren, Governor of Florida

The Colorful Western Hemisphere: Movies by
Dr. Gilberto García Cepero, Habana, Cuba

Thursday, March 30

9:00 a.m.: Presiding officers: Dr. Antonio Torres Estrada, México D. F., Mexico; Dr. Brittain Payne, New York

Transforming Individuals Through Cosmetic and Plastic Surgery
Dr. Alston Callahan, Birmingham, Ala.
Discussants: Dr. Norman L. Cutler, Wilmington, Del.; Dr. Pedro García Nocito, Buenos Aires, Argentina; Dr. Otis S. Lee, Iowa City

SYMPOSIUM: SECONDARY GLAUCOMA
Moderator: Dr. F. Bruce Fralick, Ann Arbor, Mich.

Glaucoma Secondary to Cataract
Dr. Ralph O. Rychener, Memphis, Tenn.

Glaucoma Secondary to Uveitis
Dr. William B. Clark, New Orleans

Glaucoma Secondary to Trauma
Dr. William S. Knighton, New York

Congenital Glaucoma
Dr. Saul Sugar, Detroit
Discussants: Dr. R. Bellido-Tagle, Lima, Peru
Dr. Paul Arganaraz, Buenos Aires, Argentina
Dr. Feliciano Palomino Dena, México, D. F.
Dr. Enrique Graue, México, D. F.

Provocative Drinking Tests as an Indication for Surgery in Glaucoma
Dr. Santiago Barrenechea, Santiago, Chile
Discussants: Dr. Julio Raffo, Lima, Peru; Dr. Peter Kronfeld, Chicago

Clinical Use of D-Isopropyl Fluorophosphate in Ophthalmology
Dr. Olga Ferrer, Habana, Cuba
Discussant: Dr. Charles Bahn, New Orleans

12:00 Noon: Luncheon: Presiding: Dr. Tomas R. Yanes, Habana, Cuba

When Prevention Fails—Then What?
Mr. M. Robert Barnett, of American Foundation for the Blind

2:00 p.m.: Group discussions

PROTECTING THE EYES OF THE SCHOOL CHILD

Room A: Finding the Child with Eye Defects
Leader: Richard G. Scobee, M.D., St. Louis
Discussants: Helen E. Weaver, R.N., New York; Frances E. M. Reed, M.D., Jacksonville, Fla.; Mrs. Ben Humphries Gray, Chicago; Dr. Luis Sanchez Bulnes

Room B: Lighting the Classroom
Leader: Dr. Ray L. Hamon
Discussants: J. Fred Horn, Tallahassee; James E. Garland, Miami; A. C. Bergh, Miami

Room C: The Partially Sighted Child
Leaders: Winifred Hathaway; Marjorie A. C. Young, New York
Discussants: Laura L. Sutter, Miami; Mrs. Ruby Nowell, Tampa; Mrs. Dorethia Payne, Miami; Mrs. Preston R. Yoakley, Tallahassee; Miss Louise Pickle, Tallahassee; Shaler Richardson, M.D., Jacksonville

4:00 p.m.: Summary of Panel Discussions
Chairman: Superintendent of Schools, Miami or Miami Beach

Evening: Free

Friday Morning, March 31

RESEARCH PROGRAM

Hyaluronidase: An Aid to Local Anesthesia in Ophthalmology
Harvey E. Thorpe, M.D.

Manometria de la camara anterior del ojo
Antonio Torres Estrada, M.D.

Protein Transport in Ocular Structures
Albert M. Potts, Ph.D., M.D.; Lorand V. Johnson, M.D.; Mildred Orchen, and Doris Goodman

Effect of Recommended Human Therapeutic Doses of Microwave Diathermy on Rabbit Eyes
William B. Clark, M.D.; Bertha R. Noble, M.D.; Aleta Barbour, Ph.D.

Esotropia: A Statistical Study
R. G. Scobee, M.D.

Studies on Toxoplasma in Tissue Cultures
T. Suie Jr., M.Sc.; Jackson W. Riddle, Ph.D., M.D.; Arthur M. Culler, M.D.

Effect of Anticonvulsant Drugs on Retinal Metabolism
A. P. Gilger, M.D.; Albert M. Potts, Ph.D., M.D.; Lorand V. Johnson, M.D.

Obituaries

PLINIO H. MONTALVÁN, M.D.

Suddenly, on January 18, Dr. Plinio H. Montalván died in Habana, Cuba, at the age of 45.

After graduation at the University of Habana, he joined the medical staff of the Cuban army, and in 1930 he studied at the School of Aviation Medicine, Randolph Field, San Antonio, Texas, where he was classified as a flight surgeon. Afterward, he went to the Wilmer Ophthalmologic Institute of the Johns Hopkins Hospital, being one of the most devoted disciples of Dr. Wilmer.

He opened an office in New York but, because of heart trouble, returned to Cuba.

He is survived by his wife, Ruth Warner Montalván, a son and a daughter.

The news of his death has been deeply felt by all his colleagues.

TOMÁS R. YANES, M.D.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Glaucoma

IRIDENCLEISIS. JONAS DE ARRUDA, Arq. brasil. de oftal. **11:** 145, 1948.

Statistics are presented showing the growing popularity of iridencleisis in the treatment of glaucoma in the last few years. The author attributes the popularity of iridencleisis to the following advantages: (1) The technic is simple; (2) it affords greater safety for the eye against immediate or late complications; (3) this operation can be performed in the presence of practically any type of glaucoma, and (4) the percentage of cures is higher than has been obtained with any other surgical procedure.

M. E. ALVARO.

APPLICATION OF KOLA PREPARATION IN TREATMENT OF GLAUCOMA. E. POTEKHINA and S. SUBBOTNIK, Vestnik oftal. **26:**9, 1947.

The ingredients of Kola nuts are caffeine, theobromine, collanin and collatin. Kola has a sympatheticotonic effect by regulating the general and cerebral blood circulation, thus stimulating the central nervous system. It is effective particularly in treatment of post-traumatic migraine. On the basis of these properties of Kola, the drug was used in treatment of 25 patients with glaucoma; of these, 5 were in the prodromal stage; 6 had absolute glaucoma with severe pain; 4 had simple glaucoma, and 10, chronic inflammatory glaucoma. The patients were observed from eighteen months to three years. The dose of Kola was 1 or 2 tablets (0.5 Gm.) a day, for about twenty-five days. If the symptoms reappear, the course of treatment may be repeated two or three times.

The treatment was effective in the cases of the prodromal stage of glaucoma, as the intraocular tension was lowered without the use of pilocarpine drops; the headaches and blurring of vision disappeared. Treatment was repeated with some patients whenever subjective symptoms reappeared. In cases of chronic simple glaucoma, the relative scotoma disappeared, tension was lowered and vision was improved. In cases of chronic inflammatory glaucoma the subjective symptoms were improved, but there was no improvement in the objective findings and operation was necessary.

O. SITCHEVSKA.

A MODIFIED SURGICAL METHOD IN SECONDARY GLAUCOMA. I. KOPP, Vestnik oftal. **26:** 75, 1947.

Kopp reports on the successful use of his surgical method in 9 eyes with complete adhesions of the iris to the central corneal leukoma and a narrow peripheral ring of transparent cornea. The operation served two purposes: relief of glaucoma and restoration of vision. In this procedure the conjunctiva is separated 6 to 8 mm. from the limbus. Two

concentric incisions are made at the limbus at a distance of 1 mm. from each other, one of the incisions penetrating the anterior chamber. The narrow strip of sclera formed by the incisions is removed (sclerectomy). The opening in the anterior chamber is enlarged with scissors. DeWecker scissors are entered into the anterior chamber, and the iris is incised (iridotomy) about 6 to 10 mm.; if there is membrane behind the iris, it also is cut (iridocapsulotomy). If prolapse of vitreous is encountered, the assistant uses compression with the conjunctival flap. A continuous suture is applied.

O. SITCHEVSKA.

Lacrimal Apparatus

UNUSUAL MYCOTIC INFECTION OF THE LACRIMAL CANALICULI AND CONJUNCTIVA. H. C. DONAHUE, Am. J. Ophth. 32: 207 (Feb.) 1949.

Donahue reports a case of mycotic obstruction of the lacrimal canaliculi with involvement of the palpebral conjunctiva, with identification of the fungus Aspergillus niger as the etiologic agent. Recovery from symptoms was immediate following extrusion of a tenacious, black, viscid substance after incision of the lower punctum and pressure on the lacrimal sac. A previous case of such a fungous infection has not been described in the available literature.

W. S. REESE.

AN ADVOCACY OF EXTERNAL DACRYO-CYSTORHINOSTOMY. F. N. SHUTTLEWORTH, Brit. J. Ophth. 33: 183 (March) 1949.

This report is based on 60 cases of dacryocystitis treated by external dacryocystorhinostomy. The purpose of the author is to show that the exact technic is not of very great importance and that the operation can be undertaken with equally good results by the less experienced ophthalmologists. The results are good whether an exact anastomosis between the nasal mucous membrane and the remains of the sac is achieved or not. Regular syringing for a time after the operation has value.

W. ZENTMAYER.

Lens

EARLY AMBULATION OF POSTOPERATIVE CATARACT PATIENTS. S. C. SMITH, Texas State J. Med. 43: 183 (July) 1947.

Smith says that, although the early ambulation of patients after cataract extraction is a departure from the conventional, this procedure was carried out on a series of 60 unselected patients during 1946 with results comparable to those obtained with prolonged bed rest and quiet. In all cases a monocular dressing was applied immediately after operation and the patients were allowed out of bed from sixteen to twenty hours later. The nursing problem was practically nil. The patients for the most part looked after themselves, and because of the monocular dressing the hysterical problem sometimes seen was not encountered. The fact that no prolapse of the iris ensued and that the anterior chamber quickly reformed, and for the most part stayed

reformed, may be attributed to the high conjunctival flap and the excellent coaptation of the limbal wound obtained by the Daily scleral-conjunctival technic. J. A. M. A. (W. ZENTMAYER.)

MEASLES DURING PREGNANCY AND CONGENITAL CATARACT OF THE NEWBORN ACCOMPANIED WITH A DIGITOOCULAR PHENOMENON. A. FRANCESCHETTI, Ophthalmologica **114:** 332 (Oct.-Nov.) 1947.

The author noted rubbing of the eyes with the fingers in children with congenital cataract due to measles, particularly in poor illumination, and in infants with complete cataract. The author recommends discission as soon as possible, before nystagmus develops. He offers in explanation of the etiology the fact that the measles virus is ectodermotropic and therefore attacks the lens. H. P. KIRBER.

Methods of Examination

SLIT-LAMP EXAMINATION OF THE VITREOUS AND THE FUNDUS. H. GOLDMANN, Brit. J. Ophth. **33:** 242 (April) 1949.

The method used by Goldmann consists in reducing as much as possible the angle between the illuminating arm and the microscope of the slit lamp by means of a special prism and in eliminating the refraction of the cornea. The author obtains this result with the help of a contact glass made of plastic. Instead of a contact glass, Lemoine and Valois, and later Hruby, used a concave lens of 55 D. in front of the eye. The contact glass affords a large field of vision; in general the fundus is clearer when observed with a magnification of 20; the glass can be centered on the eyeball very easily. The technic of observing a given point in the fundus stereoscopically is explained. Examination with the slit lamp has its greatest value in study of papilledema, retinitis centralis serosa and edema of the retina, and in differentiation of little spots of capillarosis from drusen and of serous and solid detachment of the retina. A number of colored plates illustrate the text.

W. ZENTMAYER.

Neurology

OCULAR MYASTHENIA GRAVIS. J. V. LISMAN, Am. J. Ophth. **32:** 565 (April) 1949.

Lisman reports 2 cases of myasthenia gravis in which the diagnosis was not apparent until after the injection of neostigmine. The signs were localized to the eyes, and in 1 case, to only one of the extraocular muscles. In the second case the appearance was that of complete external ophthalmoplegia. W. S. REESE.

OCULAR MANIFESTATIONS OF NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S DISEASE). J. FRANÇOIS, Ann. d'ocul. **181:** 753 (Dec.) 1948.

The author reviews the general symptomatology and pathology of neurofibromatosis (Recklinghausen's disease). The ocular symptoms of neurofibromatosis of the central nervous system are described. Neurofibromatosis of the lids, orbit, optic nerve, conjunctiva, sclera, cornea,

choroid and retina are then discussed in turn. The article is the best review of neurofibromatosis to appear in an ophthalmic journal in the past few years. There are 361 references. P. R. McDonald.

Orbit, Eyeball and Accessory Sinuses

Our Present Knowledge of Exophthalmos and Its Surgical Treatment. H. C. Naffziger, Ann. West. Med. & Surg. 2: 397 (Sept.) 1948.

Naffziger demonstrated that ocular protrusion is due to great enlargement of ocular muscles. A decompression of the bony orbit prevents further progression. The pathologic changes responsible have been confirmed by many, and the treatment has been widely followed in many clinics. Orbital decompression, although carrying little risk, is a procedure of such magnitude that it is reserved for conditions of considerable gravity. It has been performed in 39 cases, in many after long observation and efforts at medical treatment. In these cases the indications for operation were threatened loss of vision from danger to the cornea, choked disks or unchecked progression of proptosis which had reached the danger point. The surgical treatment consists in enlarging the orbital space to accommodate an increased mass of tissue. The use of thyroid or thyroid and iodine in the treatment of progressive disease seems to be of some help in controlling the progression and in promoting water excretion and lessening its storage, though the results are not striking. Efforts at reducing the function of the pituitary gland by the use of high voltage roentgen therapy have given varying results. Spinal puncture and administration of diuretics have accomplished little in the presence of orbital edema. Locally, sponge rubber compression pads may be worn at night to lessen the congestion and additional swelling noted after a night's sleep. Limitation of fluids has been of help.

J. A. M. A. (W. Zentmayer.)

Vascular Action of Pilocarpine, Eserine, Adrenaline and Atropine, and Their Influence in Primary Chronic Glaucoma. G. Cristini, Brit. J. Ophth. 33: 228 (April) 1949.

Pilocarpine and physostigmine determine vasodilation and the opening of new capillary districts, followed by an increase in the capillary bed without, however, dilation of the large vessels. In the light of general knowledge of hemodynamics, this causes an increase in the sum of resistances in the circulation, in spite of a considerable enlargement of the circulatory bed. The fundamental corollary to this action is the fall of the mean capillary hydrostatic pressure, and therefore of the ocular tension, such as occurs in primary chronic glaucoma. Atropine determines dilation of the large vessels without any corresponding capillary dilation and without opening up new vascular districts. According to the laws of hemodynamics, this brings about a diminution in the sum of resistances in the circulation, and therefore an increase in the mean capillary hydrostatic pressure, whenever the capillary bed, as in chronic glaucoma, is severely impaired and is no longer able to cope with such difficulties. Epinephrine determines dilation both of

the large vessels and of the smaller capillaries, followed by the opening of new vascular districts and by an enlargement of the circulatory bed. Like atropine, this drug dilates the large arterial vessels, thus diminishing the sum of resistances; but, like pilocarpine and physostigmine, it opens a new vascular reserve section, thus increasing the capillary surface. But the final effect is the increase in the sum of resistances owing to the enlargement of the capillary bed, thus bringing about a decrease in the mean capillary hydrostatic pressure, and therefore of ocular tension. W. ZENTMAYER.

Pharmacology

MYDRIATIC AND CYCLOPLEGIC ACTION OF A NEW PREPARATION, "CICLOPLEGINA." FRANCISCO PERRI, Arq. de biol. **32:** 129 (Nov.-Dec.) 1948.

The author presents a summary of the various mydriatics which have been used in ophthalmology up to the present day. He then presents his experiments with "cicloplegina." A 3 per cent solution was used. He reaches the following conclusions: 1. "Cicloplegina" provides complete mydriasis within twenty to twenty-five minutes. 2. Maximum duration of mydriasis is about twenty-four hours. 3. Complete cycloplegia is obtained within fifteen to twenty minutes. 4. Cycloplegia lasts for four hours, the maximum duration being eight hours. 5. A 2 or 6 per cent solution of pilocarpine has no miotic power in eyes under mydriasis with a 3 per cent solution of "cicloplegina." 6. "Cicloplegina" does not alter intraocular tension. Thirty case histories are given showing the action of "cicloplegina" on intraocular tension, its mydriatic and cycloplegic effects and the action of a 6 per cent solution of pilocarpine on mydriasis produced by the drug. M. E. ALVARO.

Refraction and Accommodation

HIGHER REFRACTIONAL ANOMALIES: THE FREQUENCY IN DIFFERENT GROUPS AND COUNTRIES. E. SCHMERL, Am. J. Ophth. **32:** 560 (April) 1949.

Schmerl presents a number of statistical statements and clinical observations for the purpose of demonstrating (1) the correlations which exist between higher refractional anomalies and the factors of nationality, constitution and sex, and (2) the differences in frequencies of higher refractional anomalies which exist in different parts of the world. It is hoped that this contribution will stimulate better and more specific studies in the field of constitutional ophthalmology. W. S. REESE.

Retina and Optic Nerve

EFFECT OF HESPERIDIN METHYL CHALCONE (VITAMIN P) ON DIABETIC RETINOPATHY. F. B. PECK and M. MANN, Am. J. M. Sc. **217:** 277 (March) 1949.

A group of diabetic patients were studied to determine the effect of vitamin P on diabetic retinopathy. In about 50 per cent of the cases

of retinopathy in this group the capillary permeability was increased, as manifested by the petechial index. The petechial index improved in many cases after the administration of a vitamin P preparation, suggesting that this vitamin has some effect on the capillaries. In most cases in which this effect was observed there was no significant alteration in the appearance of retinal hemorrhages. Retinal hemorrhages are seen in diabetic patients who do not show increased capillary fragility. In a majority of cases of diabetic retinopathy, vitamin P did not alter the course of the disease. In 6 cases the lesions progressed; in 5 they showed improvement, while in 5 others the vitamin was of benefit, since no fresh lesions appeared. Any favorable effect attributed to vitamin P must take into consideration the possibility of spontaneous changes in retinal lesions of diabetes.

W. ZENTMAYER.

RETROLENTAL FIBROPLASIA IN PREMATURE INFANTS. W. C. OWENS and E. U. OWENS, Am. J. Ophth. **32:** 1 (Jan.) 1949.

The authors found no retrolental fibroplasia at birth in 218 infants whose weight at birth was less than 4½ pounds (2,040 Gm.). Of these children, 111 were followed for six months or more, and retrolental fibroplasia developed in 5 of this group. The development of retrolental fibroplasia was followed in 9 premature infants. All visible remains of the hyaloid membrane had disappeared before the onset of the disease. The initially normal fundus was replaced by angiomatous dilatation of the retinal vessels, followed by massive retinal exudation, retinal detachment and the formation of a retrolental membrane by fusion of the peripheral folds of detached retina.

W. S. REESE.

SIGNIFICANCE OF OCULAR TENSION IN HEMORRHAGE OF THE FUNDUS OF THE EYE. P. WEINSTEIN, Am J. Ophth. **32:** 230 (Feb.) 1949.

Weinstein concludes that general and local factors are responsible for hemorrhages of the fundus of the eye. Among the general factors are increased blood pressure, diminished elasticity of the vessel walls and dilatation of the capillaries. The local factor responsible for the hemorrhages is decreased ocular tension. Hemorrhage of the fundus of the eye occurs when dilated retinal capillaries are associated with low intraocular pressure.

W. S. REESE.

A NEW APPROACH TO SOME PROBLEMS OF RETINAL VASCULAR DISEASE. J. S. FRIEDENWALD, Am. J. Ophth. **32:** 487 (April) 1949.

Friedenwald, in this Jackson Memorial Lecture, considers the histologic changes in the retinal vessels responsible for various ophthalmoscopic findings. He uses the demonstration of fixed carbohydrate recently refined by Hotchkiss and McManus and points out that many of the small red spots are small capillary aneurysms. Cotton wool spots seen in diabetic retinopathy are bound to be ischemic infarcts, presumably resulting from arteriolar spasm. He describes the technic used.

W. S. REESE.

INJECTION OF THE RETINAL VASCULAR SYSTEM IN ENUCLEATED EYES. I. C. MICHAELSON and H. F. STEEDMAN, Brit. J. Ophth. **33:** 376 (June) 1949.

The authors describe a method of injecting the retinal vascular system in the freshly enucleated eye and indicate the possible usefulness of this new technic.

W. ZENTMAYER.

DETACHMENT OF THE RETINA IN YOUNG MYOPIC PERSONS. S. SCHIFF-WERTHEIMER, J. JONQUERES and C. JARRY, Ann. d'ocul. **182:** 13 (Jan.) 1949.

The authors reviewed their cases of retinal detachment treated surgically between 1939 and 1948. In this series there were 49 myopic patients under 30 years of age. This group comprised about one twentieth of the patients operated on during this period. The degree of myopia varied from 6 to 20 D., the average being about 12 D. In most patients the detachment occurred without prodromal symptoms. Four gave a history of a minimal degree of trauma preceding the visual symptoms. One of the characteristics of the retinal detachment is the presence of numerous tears. An average of two to three tears was observed. Disinsertions, when present, were large and at times involved one-half the retina. Redetachments were common after operation, and in many instances bilateral detachments developed. Of 46 patients who were followed, bilateral detachments developed within a year in 15. In the authors' series, operation resulted in complete failure in 47 per cent; a good anatomic result was obtained but vision was less than 1/10 in 18 per cent, and a good anatomic result with vision of better than 1/10 was obtained in 34 per cent. The prognosis is much poorer for the young myopic person than for an older one with the same degree of myopia.

P. ROBB MCDONALD.

THE RETINAL HOLE WITHOUT SYMPTOMS. E. WEBER, Ophthalmologica **114:** 305 (Oct.-Nov.) 1947.

Frequently retinal holes are seen in the extramacular area of patients with high myopia which have not caused detachment. The author advises surgical treatment of these eyes if (1) there is detachment in the other eye or (2) if the hole is in the upper segment. He advises delay in operation when the hole is in a lower segment, since he has seen many spontaneous healings in such cases.

H. P. KIRBER.

PROPHYLACTIC OPERATION FOR DETACHMENT OF THE RETINA. A. FRANCESCHETTI and C. BALAVOINE, Ophthalmologica **117:** 259 (April-May) 1949.

The authors discuss the question whether a prophylactic operation is justified in cases in which a retinal hole is found and no detachment is present. In 1947 Weber advised immediate operation under the following conditions: detachment of the retina in the fellow eye, when the hole is located in the upper quadrant; progressive degeneration of the retina; myopia, and a hereditary disposition. To these indications the authors add that in young adults surgical intervention is justified because extensive degenerative changes are frequently present;

a further indication is in cases in which the periphery of the retina cannot be seen, e. g., those in which the pupil does not dilate or in cases of ectopia lentis. Several cases are described and statistics cited from the literature.

H. P. KIRBER.

PLACENTA IMPLANTATION AND NICOTINIC ACID IN TREATMENT OF RETINITIS PIGMENTOSA. A. MOGINIER, Ophthalmologica **117:** 287 (April-May) 1949.

Small pieces of fresh placental tissue are implanted subconjunctivally once or twice over a period of three months. The local reactions are negligible. Thirteen patients were treated, of whom 8 showed improvement. These were young persons with an initial visual acuity of at least 0.5. The visual acuity and fields were improved; dark adaptation was unchanged. Four patients were treated with nicotinic acid for prolonged periods, with similar results. The explanation is offered that nicotinic acid and placental hormones act as vasodilators and thus improve the metabolism of the retina. No case histories are presented. In the discussion of the paper, Pascal said that the Russian reports on treatment with placental implants could not be confirmed when repeated in the United States.

H. P. KIRBER.

Therapeutics

STERILIZATION DOSAGE, RADIATION AND NEW TYPE HANDLE FOR THE RADIUM-D OPHTHALMIC APPLICATOR. H. SWANBERG, Mississippi Valley M. J. **70:** 238 (Nov.) 1948.

Swanberg has found two antiseptics that apparently have no effect on the aluminum filter used in the application of radium D. They are "S. T. 37 antiseptic solution" (hexylresorcinol, 1:1,000, in a glycerin-aqueous solution) and 70 per cent antiseptic alcohol. The alcohol should be washed off with sterile water. R. D. Evans, who has studied the radiation from a number of applicators, states that the latter are the source of substantial pure beta radiation and a small amount of feeble, low energy gamma radiation. A new type of applicator handle is described.

W. ZENTMAYER.

RETROBULBAR INJECTIONS OF SODIUM CHLORIDE SOLUTION IN OCULAR THERAPEUTICS. MARIO DEL GIUDICE, Rev. brasil. oftal. **7:** 69 (Dec.) 1948.

The author, seeking a rapid method of therapy for ulcerous keratitis, decided to try the treatment used by internists for ulcers and cutaneous wounds, namely, subcutaneous injections of autoserum around the ulcers. He gave subconjunctival injections of autoserum, but these were poorly tolerated and the retrobulbar route was then used. He found that, in addition to the good results obtained with the ulcers, these injections also had a hypotonic effect in eyes with increased intraocular tension. He later substituted for the autoserum a 1 per cent solution of sodium chloride and obtained the same results. To allay the pain of these injections, a 1 per cent solution of procaine hydrochloride was added. The results have been satisfactory.

M. E. ALVARO.

Uvea

ESSENTIAL PROGRESSIVE ATROPHY OF THE IRIS. M. A. LASKY, Am. J. Ophth. **31**: 1131 (Sept.) 1948.

Lasky reports a case of essential atrophy of the iris in a woman aged 22 on whom he later operated for glaucoma three times without success. He reviews the theories of essential atrophy of the iris.

W. S. REESE.

Visual Tracts and Fields

BINASAL HEMIANOPSIA. M. B. RAIFORD, Am. J. Ophth. **32**: 99 (Jan.) 1949.

Raiford discusses binasal hemianopsia and reports 2 cases in which the field defect was due to a tumor. The presence of one tumor was verified by operation, and the second had apparently metastasized from the lung.

W. S. REESE.

ALTITUDINAL HEMIANOPIA DURING STREPTOMYCIN THERAPY. A. E. SCHULTZ, Am. J. Ophth. **32**: 211 (Feb.) 1949.

Schultz reports a case of altitudinal hemianopsia in a tuberculous patient during streptomycin therapy. Streptomycin toxicity, air embolism and angiospasm are given as possible causes. Therapy was based on the premise that a thrombus or an embolus produced partial obstruction in the trunk of an inferior retinal artery. Complete visual recovery was obtained.

W. S. REESE.

Vitreous

USE OF STERILE REFRIGERATED POOLED HUMAN VITREOUS IN LIVING EYES. M. H. FRITZ, Am. J. Ophth. **32**: 45 (Jan.) 1949.

Fritz states that it is established that aspiratable portions of the vitreous of enucleated human eyes may be pooled and kept indefinitely. He suggests that the collection, storage and distribution of such vitreous be administered by eye banks.

W. S. REESE.

Society Transactions

EDITED BY DR. W. L. BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

W. Guernsey Frey, M.D., Chairman

Maynard C. Wheeler, M.D., Secretary

Regular Meeting, Feb. 16, 1948

INSTRUCTION HOUR

Office Bacteriology. DR. FREDERICK THEODORE.

PAPERS OF THE EVENING

Atypical Form of the Syndrome of Foville (Paralysis of Lateral Gaze). PROF. GAETAN JAYLE, Marseilles, France (by invitation).

Association of paralysis in one eye and nystagmus in the other when the subject is looking laterally was described as the atypical form of Foville's syndrome.

The findings in 7 cases, personally observed by the author, were described and presented graphically by means of ingenious diagrams.

The manifestations may be divided as follows: (1) the chief sign, association in lateral gaze of paralysis of either the internal rectus muscle (internal form) or the external rectus muscle (external form) and nystagamus of the other eye; (2) secondary manifestations, such as disturbances of mobility in the vertical plane and spontaneous nystagmus; (3) disturbances of experimental vestibular mobility. These disturbances are always present in the plane of the chief sign; in the two other planes they vary in each case, and may be absent.

In attenuated forms of the syndrome the paralysis of the affected eye is a paresis. A most attenuated form is the bilateral asymmetric nystagmus. A relation exists between the pure Foville syndrome and the monocular nystagmus of the external rectus muscle in lateral gaze, on the one hand, and the supranuclear paralysis of the internal rectus muscle, on the other. The intermediate form is the atypical form of Foville's syndrome.

Multiple sclerosis has been given as the cause in all but 1 of the 32 cases in the literature, but the correctness of this incidence is controversial. In the diagnosis of multiple sclerosis, the atypical form of the Foville syndrome is not as significant as retrobulbar neuritis, but it is certainly an important element in the differentation.

Treatment of Superficial Corneal Injuries. DR. A. RUSSELL SHERMAN, Newark, N. J.

Corneal epithelium tends to regenerate rapidly. The logical treatment of any corneal injury in which loss of epithelium is the chief feature is one which encourages regeneration of epithelium. This can best be

accomplished by preventing movements of the lids and eyes by bandaging both eyes—a procedure which has given satisfactory results in treating injuries due to lime and other chemicals, as well as those produced by finger nails, twigs and similar objects.

Twenty patients with corneal defects amounting to from one fourth to three fourths of the corneal surface were treated in this manner, with recovery in three to five days. Similar injuries treated by compresses and frequent applications of anesthetics and antiseptics have often taken several weeks to heal, and then with visual impairment resulting from scar formation; scarring does not occur if healing is rapid.

DISCUSSION

Dr. Arthur Knapp: Dr. Sherman's paper is very interesting, but it might be well to mention our experience at the New York Navy Yard, Brooklyn, during World War II, which was reported in *The Journal of the American Medical Association*. Among more than 70,000 employees, 52,704 injuries were reported in 1944, with 11,380 ocular accidents. There were many superficial foreign bodies in the cornea. After removal of the foreign body an anesthetic ointment was instilled into the lower cul-de-sac. The patient was given a small tube of the anesthetic to place in the eye at the onset of the slightest pain. He also received 15 grains (0.975 Gm.) of acetylsalicylic acid. Healing was in no way interfered with. The patient returned to work directly and continued with binocular vision.

Dr. Willis S. Knighton: Has Dr. Sherman had complicating conjunctivitis as a result of keeping the eyes closed for a considerable time?

Dr. Joseph Fried (by invitation): What is Dr. Sherman's feeling about binocular bandaging for injuries in the upper and lower fornices?

Dr. Maurice Landau, Rochester, N. Y. (by invitation): Has Dr. Sherman had any experience with use of ointments containing vitamin A and vitamin D in these cases?

Dr. Henry Dubins, Albany, N. Y. (by invitation): I wonder whether the use of the pinhole disk for immobilization would be as effective as tight bandaging.

Dr. A. Russell Sherman: I believe that my treatment is based on logic. It is not original. In Fuchs's textbook, Duane states that in cases of recurrent erosion eyes must be bandaged for one or two weeks, or longer.

I was not including in these cases any of injury from ordinary foreign bodies; those injuries I treat in much the same way as does Dr. Knapp. I make no attempt to produce binocular, or even monocular, occlusion in a patient who has a superficial or an embedded foreign body.

My patients were considered to have superficial injuries. Those who had injuries to the fornices usually had severe injury of the cornea, so that their lesions would not be classed as superficial. I showed a slide of a patient with a rather severe burn of the conjunctiva of the upper lid, sufficient to cause scar tissue with deformation of the eyelids; by and large, however, none had any involvement of the fornix. I am surprised that in no case was there conjunctivitis from occlusion. When I first began to treat lime burns accompanied with a considerable secretion of mucopurulent material, I was hesitant to bandage the eye firmly,

but the conjunctivitis subsided instead of becoming worse. The conjunctivitis is not usually of the infectious kind; rather, it is of the type that follows use of silver nitrate. The conjunctiva is fairly sterile because the caustic agent takes care of the organisms present, and if the ophthalmologist does not introduce new ones there will be no infection.

I do not think that the pinhole disk would be effective, for the patient would be opening and closing his lids, and the purpose is to keep the lids quiet.

I can see no reason for using preparations of vitamin A or D. Certainly, in this part of the world patients have enough vitamin A and D in their systems. If we cover the eye for a few days and give the cornea a chance to heal, it will do so. My idea has been to give nature the opportunity to take care of the injury.

The Vitreous: Its Pathologic Histology and Examination with the Slit Lamp. Prof. Karl Lindner, Vienna, Austria (by invitation).

The structure of the vitreous is ultramicroscopic. In addition, it possesses a kind of microscopic structure which becomes recognizable by the arrangement of blood cells when they infiltrate it. The comparison of a microscopic onion-like structure of the vitreous to Liesegang rings is erroneous.

With age the vitreous becomes increasingly liquefied in its center and the cortex becomes thinner. A posterior detachment of the vitreous develops in all cases of perforating injuries or operations, as a result of the shrinking of the vitreous. In young persons the shrinking vitreous becomes detached up to the ora serrata; in older persons it remains adherent to the anterior parts of the retina. As the retina and the choroid are a physiologic unit, the shrinking of the vitreous causes choroidal detachment in older persons, but it is invisible in young persons because it is more anterior. All this can be seen in microscopic sections.

The examination of the vitreous and of the fundus has been facilitated in recent years by the lens of Hruby. This is a high minus lens (+ 5 D. sph. ⊃ — 60 D. sph.) which is placed before the patient's eye instead of a contact lens. The Goldmann slit lamp is the best type for this examination. The slit lamp and microscope are on one stand and are moved simultaneously with one hand in all directions. Hruby's glass and fixing lamp are attached to the slit lamp, and the patient's eye can be moved in any direction while the instrument is focused as desired. This arrangement allows the examination of the eye after recent operation and of eyes of nervous patients and of children.

Professor Lindner then showed a series of pictures of the vitreous and of the fundus which explained the connection between the detached vitreous and the retinal detachment.

DISCUSSION

Dr. George Kleefeld (by invitation): It may be of interest to recall a few of the earlier developments: The idea of using a powerful concave lens instead of a contact lens has been already realized by two French oculists, Lemoine and Valois.

Beginning about the second half of World War I, a man of genius, Leonard Koeppe, devoted years of a feverish activity to the study of

Gullstrand's slit lamp and its application to the examination of the anterior, as well as the posterior, segment of the eye. For study of the latter he had designed a contact lens. The beam of light issuing from the terminal lens of the slit lamp had to be reflected on a front-surfaced mirror in order to reach the deeper parts of the eye in such a way that the axis of illumination and the axis of observation formed an extremely acute angle.

The so-called corneal microscope, or Czapski's microscope, was binocular. It carried double objectives the width of which was about 35 mm. and the height 12 mm. The mirror could not be brought close enough to the axis of observation without covering one of the objectives. Thus, binocular observations became impossible. To overcome this difficulty, Koeppe had to substitute a special type of binocular microscope, with only one thin objective. This microscope gives an inverted image.

In the course of my optical studies, I redesigned the front-surfaced mirror. The new mirror, independent of the terminal lens of the slit lamp, could be given any desired position. In addition, I found that a change in the position of the slit lamp was sufficient, without necessitating a special microscope for examination of the vitreous body and retina in the focal beam of the slit lamp. The slit lamp, instead of being disposed horizontally with the mirror touching the side of one objective, should be directed vertically—the housing up, the terminal lens down and the mirror touching by its lower border the upper border of the double objectives. A stand having the shape of a gallows had to be attached to the elevating mechanism, at the end of the double arm. The slit lamp, with the mirror, had to be "hung" at the extremity of the horizontal branch of the gallows. This mirror could be oriented at will, without covering either objective. It could be used with the most powerful objectives.

According to Koeppe, the use of a prism instead of a mirror would not be in agreement with the principle of the Gullstrand slit lamp.

I agree entirely with Professor Lindner that the use of the contact lens for examination of the vitreous body and the fundus is sometimes dangerous, as, for example, in case of detached retina. Besides, some patients are not cooperative. For this reason, I pursued my studies of the vitreous body and the fundus by using the so-called Gullstrand simplified ophthalmoscope, with the focalizing device of Zamenhof. This instrument consists of a narrow lens of 32 D. which slides along a short arm. It projects the image of the slit lamp in the fundus of the eye through the upper part of the ophthalmoscopic lens, so that this linear image can be observed with the monocular or binocular attachment of the Gullstrand ophthalmoscope. The slit can be focused on the fundus or on any opacity existing in front of it. The relation between fundus and vitreous body can then be studied. The Zamenhof method permits the examination of the vitreous in the upper half of the globe, with the eye looking straight ahead. I designed a rotating stand wherewith the simplified ophthalmoscope could be placed upside down, so that the lower part of the eye could be observed under the same conditions. In order to record photographically the opacities of the vitreous body, I used the Nordensen retinograph. The carbon arc

light had to be pulled backward as much as possible, so that the spot of light should appear in the middle of the vitreous body. Additional convex lenses were used for the same purpose.

In summary, after having modified the Koeppe method in 1922, I used the so-called Gullstrand simplified ophthalmoscope with removable refractometer and Zamenhof focalizer to build up a complete method of exploration of the vitreous body which does not require either a contact lens or a concave glass in front of the eye.

Dr. Henry Minsky: I should like to ask Professor Lindner whether the normally disposed retina in front remains in contact with the vitreous because the hyaloid membrane is intact, and whether the posterior part of the retina does not remain attached because the hyaloid membrane is diseased. What is his opinion concerning the effective pull of the ciliary muscle in the mechanism of spontaneous detachment of the retina?

Prof. Karl Lindner, Vienna, Austria: The history of the examination of the vitreous is to be found in my articles. The patient cannot stand the examination with the Koeppe method. Zamenhof showed me his instrument, but it is quite different; with his device, it is as though one used the ophthalmoscope instead of a real instrument with the arc lamp to make an examination with the red-free light. I am glad that someone else has found a way to examine the vitreous. The main question is whether the method is practical. The instrument described is a handy one, the patient is seated, and he has nothing to do; one puts the instrument in front of his eye and guides him. Some of my colleagues believe that one sees better with a contact lens. I thought at first that I saw still better with the contact lens and monocular angular microscope, but I now know that I do not. Dr. Hruby, when in Switzerland, demonstrated to Goldmann that he could see all the details with his lens just as well as Goldmann could see with the contact lens. The mirror of Koeppe is not convenient. It is difficult to place the beam correctly, and nowadays no one uses it. It is often that a slight modification in the examination causes great progress. The prism of Goldmann is not a mirror; it leads the beam of light in the right direction, but it does not reverse it.

An answer to Dr. Minsky's questions would carry us too far from the subject under discussion.

W. Guernsey Frey, M.D., *Chairman*

Maynard C. Wheeler, M.D., *Secretary*

March 15, 1948

INSTRUCTION HOUR

Virus Diseases of the Eye. Dr. Alson E. Braley (by invitation).

PAPERS OF THE EVENING

The Alarm Reaction in Relation to Scotometry. Dr. Mortimer Cholst (by invitation).

The effect of acute apprehension on angioscotometric determinations was reported in 3 cases. In 1 case, that of a hospital patient, the normal

angioscotoma had already been mapped, when he suddenly became very apprehensive, as a result of a message from his home. In the other 2 cases the patients were examined in the emergency room, immediately after a chemical explosion, while they were extremely frightened. All these patients had their angioscotomas remapped after they had received reassurance which dispelled their apprehension. The findings were essentially the same in all cases: a decided widening of the angioscotoma while the patient was in the state of alarm, with gradual narrowing of this band after reassurance, until the accepted normal dimensions were reestablished.

The possible physiologic mechanism involved in the production of this widening of the scotoma in fright could be the liberation of an epinephrine-like substance. According to the literature, such a substance increases the venous pressure, with resulting increased cerebrospinal fluid pressure. This increased intracranial pressure interferes with the normal drainage of the intraocular tissue fluids posteriorly, causing dilatation of the perivascular spaces. The back pressure that ensues interrupts the synapses in the underlying retina, owing to the edema produced. There is thus a loss of response of the rods or cones of the corresponding neurons, and widening of the angioscotoma results. The disappearance of the psychic stimulus is followed by a reversal to the normal physiologic state, restoration of which can be noted clinically by replotting the normal angioscotoma.

In conclusion, this effect of fright may perhaps be a source of error in the mapping of the blindspot when routine plotting of the central scotoma is performed on patients in an apprehensive state.

DISCUSSION

DR. CHARLES A. PERERA: I should like to ask Dr. Cholst whether two factors have been considered: One is the attention of the patient. In the plotting of angioscotomas, close attention and cooperation are necessary; I wonder whether the patient's lack of attention due to his thinking of other things may not have been a factor in the change of the scotoma. The second point is whether the author studied a patient who had never before had an angioscotoma plotted and then mapped a series of angioscotomas at short intervals. Will the angioscotoma be larger, and then become smaller as the patient becomes adapted to this procedure?

DR. MORTIMER CHOLST: Dr. Perera's questions are well founded. Numerous studies have been made, especially at the Long Island College Hospital, under the supervision of Dr. Evans, to determine the importance of these sources of error. Angioscotomas were plotted on inattentive, as well as on fresh, patients, and it was found that these factors could be ruled out.

Primary Epithelial Tumors of the Ciliary Body. DR. J. A. C. WADSWORTH (by invitation).

In order to facilitate the discussion, a classification of the primary epithelial tumors according to their type and degree of malignancy was presented. The four types of epithelial tumors of the cilliary body and

their relative frequency were discussed, and the microscopic picture was described. It was possible to establish the relationship between the small, so-called benign adenomas of the ciliary body and the malignant epitheliomas seen in this region of the globe. The author stated the belief that small adenomas have a malignant potentiality and bear no significant relation to previous inflammation in the globe. Through a study of a large series of cases of these tumors, the author reconstructed the manner of their formation and traced the development from the small, so-called benign lesion into a large, malignant tumor destroying the structures of the ciliary body and infiltrating into the iris and the anterior chamber. Statistical studies were made of cases presented in the literature and the figures compared with those for the author's series. The embryonic type of tumor was also discussed and compared with the adult types, as well as with the retinoblastoma. Two cases were presented in which both clinical and pathologic studies were made. It was concluded that the small, benign epitheliomas were potentially malignant, but that in no case had the tumor been found to extend outside of the globe. The embryonic type of epithelial tumors had the characteristics of a retinoblastoma.

Simple Graphic Recording of Ocular Lesions. DR. HENRY MINSKY.

Dr. Minsky presented a detailed scheme for describing and locating lesions in and around the eye by means of simple diagrams, letters and numbers. This is a sort of shorthand that Dr. Minsky has evolved for his own records. It should enable ophthalmologists to keep more complete records in much less time than is required for the usual written descriptions.

Ocular Findings in Three Hundred and Twenty-Three Patients with Schizophrenia: A Preliminary Report. DR. MARTIN COHEN.

This paper was published in full in the June 1949 issue of the ARCHIVES, page 697.

DISCUSSION

DR. NOBE E. STEIN (by invitation): I am not an ophthalmologist and do not feel competent to comment on Dr. Cohen's ophthalmologic findings. Schizophrenia is a serious social and medical problem. The etiology of this mental illness has been the subject of much research and discussion. Many theories have been advanced, but so far nothing definite has been established. Both physical and psychologic factors appear to play a part. Kraepelin, in 1897, advanced the theory of autointoxication; this was later refuted by European and American workers. Bleuler, who introduced the term schizophrenia, approached the problem from the standpoint of an organically determined change in the associations. This theory was rather vague and not accepted readily. Cotton advocated the theory of focal infection. He removed such foci and claimed to have good results. Kopeloff and Kirby followed his plan, but using a control group, and they could see no more improvement in the treated than in the untreated patients. There is no doubt, however, that an infectious disease or chronic infection may so lower resistance

that the mental condition becomes manifest. Von Monakow presented the idea that the choroid plexus failed in its function as a selective filter and, because of the degenerative changes in the plexus, certain products of metabolism and of the endocrine glands were able to reach, and so affect, the central nervous system. Buscaino expressed the belief that the cause lay in metabolic disturbances. He found that the urine contained some amino products. Endocrine imbalance has also been advocated as a cause of this illness. Neuropathologists abroad and in this country have examined hundreds of brains of schizophrenic patients. Some have found morbid anatomic changes; others have not. I assume that you are interested chiefly in the organic phase.

When Dr. Cohen found the pallor of the disk in a high percentage of patients of the first group examined, I was inclined to attribute it to a vasospastic condition. Months later, when he rechecked the eyegrounds, the pallor was either the same or accentuated. Consequently, I suspected that his findings were most probably due to a degenerative process. However, further studies on patients with this disease and on those with other psychoses and psychoneuroses are indicated before any conclusion can be drawn. The fact that Dr. Cohen found some pathologic change in the eyegrounds in 69 per cent of schizophrenic patients may stimulate psychiatrists and neurologists to make more thorough ophthalmoscopic studies. One may properly raise the question of previous treatment with insulin, electric shock or metrazol.* Of the total number of 323 patients, 232 had lesions of the eyegrounds. Of this number, 26 had been treated with insulin, 14 with electric shock and 3 with metrazol,* a total of 43, or 18.1 per cent. Of the patients with normal eyegrounds, the percentage of those who had had similar treatment was about the same. In my judgment, the shock treatments had no bearing on the changes in the eyegrounds.

Dr. Raymond E. Meek: Dr. Cohen took me to the Manhattan State Hospital to look at the fundi of some of the patients whose cases he has presented this evening. I examined 13 of these schizophrenic patients and found an abnormal disk in every one. While I cannot say that a tawny gray discoloration accurately describes the appearance of the disks, I will say that the disks lacked the normal delicate peach tint and that in all cases the temporal side was pale and had a dirty or gray appearance. I will also say that the disks were not normal. At the hospital I pointed out that, while these disks were not those of normal persons, they might be the result of shock treatment with insulin or metrazol,* but the records showed that only 1 of the 13 patients had been so treated. All these patients had been under treatment for a long time, and it is quite possible that they received treatment privately or at another institution before entering the Manhattan State Hospital. These patients must be guided in their habits of personal hygiene, and they may be constipated for long periods; this is particularly true of the catatonic patients while in the stuporous phase. In such a large hospital, it is impossible to see that the patients get fruit juices; even when they are given a balanced diet, with greens, they may not eat it. Constipation, lack of a normal balanced diet and deficiency of vitamins might

cause this change, through general debility and secondary anemia. Practically all the patients in this hospital come from the lower strata of society and have never from birth had what one might call adequate care. I often see optic disks similar to these in the poor who frequent the clinics.

I feel that the 31 per cent of normal disks found is of great significance. This is too great a number of normal disks to permit designation of the findings as characteristic of the disease.

In a hospital such as Bloomingdale's division of the New York Hospital, where one sees patients from the upper stratum of society who are affected with this mental condition, the eyegrounds should be studied. If the same proportion of abnormal disks is found there, in persons who have had the best of food and care, greater significance might be attached to the finding.

Before definite conclusions can be drawn concerning the significance of these abnormal disks, comparisons should be made of the disks of 100 patients with schizophrenia with those of 100 patients with involutional melancholia, or even of 100 patients with the psychoneuroses, such as hysteria, anxiety hysteria or compulsive, obsessive or character neuroses, and also with the disks of 100 underprivileged persons who have never had adequate food and care.

The only way in which advances in science can be made is through the study and presentation of new ideas, and I congratulate Dr. Cohen on the difficult task he has undertaken. He may have opened new avenues into the study of the so-called functional mental diseases. They may cease to be considered functional and may prove to be actually organic.

W. Guernsey Frey, M.D., *Chairman*

Maynard C. Wheeler, M.D., *Secretary*

April 19, 1948

INSTRUCTION HOUR

Aids in the Presentation of Papers. Dr. Hunter H. Romaine (by invitation) and Mrs. Mary Brown (by invitation).

PAPERS OF THE EVENING

Neurofibromatosis Associated with Tumors of the Optic Papilla: Report of a Case. Dr. Jacob Goldsmith (by invitation).

This paper was published in full in the January 1949 issue of the Archives, page 718.

Use of Propionates in Ophthalmology: A Preliminary Report. Dr. Frederick H. Theodore.

This paper was published in full in the June 1949 issue of the Archives, page 83.

DISCUSSION

Dr. Samuel M. Peck, I congratulate Dr. Theodore on a thorough presentation. I followed his work with great interest, and I can assure you that during the period of his observations he was most careful in

all his evaluations. It may interest you to know that for years the dermatologists, bacteriologists and mycologists have been talking about the normal acid mantle on the surface of the skin. They mean by that that so long as the hydrogen ion concentration on the body surface was maintained within certain range there seemed to be resistance against infection. That was the original starting point for our research, because we were then able to show that this acid p_H over most of the body surface is due to the fact that the skin contains what may be properly called human antibiotics. Just as simple organisms like Penicillium produce an antibiotic which kills bacteria, so does the human body produce a defensive substance to kill bacteria and fungi. These are found in the normal secretions of the sweat and sebaceous glands. This is of enormous practical importance. By analyzing the sweat, we were able to determine what these fungistatic and bacteriostatic substances were. This has proved to be important in the present epidemic of fungous infection of the scalp. It had been known for many years that children had such an infection and that at puberty it disappeared, and a great many theories were advanced to account for this. It was found that at puberty the glands begin to secrete a fatty acid, which is found in the adult and not in children, and which sterilizes the hair follicles, so that there is spontaneous cure. By following the same line of reasoning, Heaven only knows where further research may lead us. I can say that we have just scratched the surface, and I do not mean to be funny! We had started with the propionates in the treatment of fungous disease when the war came along and interrupted our research. At present we are using mixtures of propionates and caprylates because these have been found more efficacious. We have many other fatty acids which can be used; some of them have an astonishingly high rate of bacteriostatic power. An important fact which emerges in a series of studies on the evaluation of fungistatic and fungicidal substance is that when organisms are killed or disease controlled by means of a fungistatic or bacteriostatic substance there is a decreased formation of toxic bacterial substances, substances which play a great role in disease symptoms. The reason for symptoms in a fungous infection is that there is a high degree of sensitization. If a fungistatic substance is used to kill the fungi, to prevent the growth of fungi and to control the disease, practically none of the substance is formed which gives rise to fungous allergy. The use of a strongly fungicidal substance increases this formation and therefore causes flare-ups in the disease. I think it applies to bacteriologic conditions as well.

I wish to stress an observation on the peculiar soothing properties of the fatty acids. A group working on vulvovaginitis noted in the treatment of diseases of the mucous membranes that the fatty acids exerted an antipruritic and partial anesthetic effect. It was proposed that the fatty acids might be soluble in the myelin sheaths of the nerves and thereby act like a local anesthetic. It is a common observation that sodium propionate used as wet dressings exerts this highly soothing effect.

I wish to thank Dr. Theodore, and I hope he continues his search for the best possible combinations of fatty acids for the treatment of infections of the eye.

Dr. Frederick Theodore: Dr. Paton, who was unable to be here tonight, was to report on his results with the use of sodium propionate. He asked me to say that his results were favorable.

Minimal Defects in Visual Field Studies. Dr. Max Chamlin (by invitation).

This paper was published in full in the August 1949 issue of the Archives, page 126.

DISCUSSION

Dr. LeGrand H. Hardy: I am happy to compliment Dr. Chamlin on a splendid piece of work in calling attention to minimal defects in the visual fields. At least two of his three criteria seem valid and are valuable to me. The device of using differences in the patient's own ocular function as a criterion in evaluating loss of field is particularly valuable, since the other criteria we have are not very reliable. There are many variables in perimetry, and the three criteria which he mentioned will be of help in revising estimates of loss derived from other standards, such as the Ferree-Rand and Walker normal field limits.

I should like to ask Dr. Chamlin about his evaluation of the 1/2,000 test object, which is an extremely difficult one to use. Ophthalmologists have been inclined to accept for international standards a central field taken with the 1/1,000 test object. Does Dr. Chamlin think he gains a distinct advantage in using a 1/2,000 test object, except in special cases, or does he believe that a 1/1,000 test object will cover the same field defects with less strain on both perimetrist and patient? Patients with cerebral tumors are usually sick people, and it is difficult for them to cooperate well enough to use minimal test objects; yet minimal test objects are the only means by which one can detect minimal defects.

Dr. Adolph Posner (by invitation): Dr. Chamlin's excellent presentation is based on carefully worked-out ideas. I should like to emphasize a point which he has already stressed. The patient often presents a psychologic problem, but one forgets the perimetrist's psychologic slant. I refer to the fact that the perimetrist tries to approximate each individual field to a certain accepted norm. This is especially true in mapping out the blindspot. To illustrate this point, it was only through careful work and judicious disregard for the conventional and typical that Evans discovered angioscotometry. One tends to think of the blindspot as a perfect ellipse. One also tends to disregard minor differences and irregularities in the rest of the field. More attention should be paid to individual differences and less to the so-called norms. Last June, in Atlantic City, I demonstrated an attachment to a tangent screen which is based on the pantograph. This device enables one to use a tangent screen without any markings and to copy the field from it on a chart. In this way, one does not have to be influenced by the assumed position and size of the blindspot. I find that this method works out satisfactorily in overcoming my own tendency to approximate.

DR. MAX CHAMLIN: I do not think that the 1/1,000 test object can replace the 1/2,000 test object. The latter is a minimal stimulus for the inner 15 or 20 degrees of the field, whereas the 1/1,000 test object, subtending twice as great a visual angle, is visible to 25 or 30 degrees without difficulty and is no longer a minimal stimulus in the inner 15 or 20 degrees of field. Certainly, some of the slight level differences and some of the slight qualitative differences brought out by "rapid comparison" on the charts shown would be missed with the 1/1,000 test, for they were just barely picked up with the 1/2,000 test object.

One cannot plot minimal field defects with sick patients. These fields were plotted with patients who were mentally alert and were hospitalized because they had headache or seizures, or perhaps because their physician found papilledema. All the minimal defects presented were found in patients who were cooperative.

What Dr. Posner says about the psychologic approach to perimetry is intriguing. Some patients are very suggestible and are easily influenced to call the readings which the inexperienced perimetrist may expect to obtain. These patients have some type of functional disturbance. One must be careful in interpreting such readings. Other patients can lead the examiner astray because they will have their own opinion on what they are seeing and not seeing, and may even influence the examiner unduly. These conditions must be considered in describing the patient's "cooperation" on the chart. If this cooperation is poor, one must be cautious in interpreting the results.

There is a tremendous variation in the so-called norms for breadth of field in different people. Ferree and Rand and Monroe have done excellent work in evaluating these differences. However, one must evaluate each case individually. For example, one may compare the smaller hemianoptic field with the larger half of the normal side, as pointed out in the slide demonstration. One must be cautious about interpreting generalized peripheral contraction, when it is very regular, as being due to pathologic conditions such as atrophy following papilledema. If peripheral contraction is very regular concentrically, it is unlikely that it is a pathologic entity. It would be rather difficult to conceive of prolonged pressure on the optic nerve causing so even a disturbance of function as to give a perfectly rounded small field. Rather, the pathologically contracted field in such a case is likely to be irregular. The very regularly contracted peripheral field is more likely to be the product of a patient who was not exerting his fullest perceptive power in the extreme periphery of the field, and the perimetrist must learn to recognize such conditions. I do not think any hard and fast rules can be made about them. Rather, one must learn to interpret bizarre findings from one's own clinical experiences.

W. Guernsey Frey, M.D., *Chairman*

Maynard C. Wheeler, M.D., *Secretary*

May 17, 1948

INSTRUCTION HOUR

Plastic Surgery of the Eye. DR. BYRON SMITH (by invitation).

REPORTS OF CASES

Reconstruction of an Eyelid. Dr. Arthur B. Duel Jr. (by invitation).

The case of a white woman aged 53 with carcinoma involving the middle third of the right upper lid was described. Nearly half of the lid had to be removed for its entire thickness. The lid was reconstructed by the method of Hughes (1945), in three stages.

Senile and Cicatricial Ectropion: Report of Three Cases. Dr. Rudolf Aebli.

The surgical treatment in 3 cases of ectropion, representing three types, was described.

Case 1.—A patient with pronounced senile ectropion with thickening and hypertrophy of the exposed palpebral conjunctiva presented an indurated, papilloma-like mass involving the outer third of the lower lid of the left eye. The Kuhnt-Szymanowski operation gave an excellent result.

Case 2.—A cicatricial ectropion of the lower lid of the left eye followed a lacerated wound. The lid margin was freed; lid adhesions were produced; the scar tissue was freely excised, and a full thickness skin graft from the upper lid was used to cover the defect. Three months later the lid adhesions were cut.

Case 3.—Cicatricial ectropion of both the upper and the lower lid of the left eye followed a severe third degree burn. During the first ten days the burned area was treated with constant wet dressings of penicillin solution, and daily the wound was cleansed and dead and sloughing tissue removed.

PAPERS OF THE EVENING

Beta Radiation in Ophthalmology. Dr. Frederick H. McKee.

The conditions in which there has been enough experience with treatment to justify a report are tabulated according to the results of therapy.

Excellent Results	*Fair or Questionable Results*
Prevention of superficial vascularization after keratectomy and keratoplasty (postoperative therapy)	Tuberculosis of the anterior ocular segment (attack is shortened and severity lessened)
Vernal conjunctivitis	Acne rosacea
Epitheliomas of eyelids, conjunctiva and cornea	Blepharitis marginalis
Recent corneal scars	Distichia
Small papillomas of the eyelids and conjunctiva	Herpes
Angioma	Postoperative scarring
Tuberculosis of the eyelids and sclera	Opacities of the cornea
Lymphoid overgrowths on the ocular conjunctiva	Trachoma
Severe keratoconjunctivitis	Interstitial keratitis
Granulations, conjunctival flaps and pterygiums, which can be made avascular	

Among the conditions which have not been benefited by any technic thus far used are lymphangioma, nevuses, cysts, malignant melanoma, corneal ulcer due to pyogenic infection, old calcified corneal scare, punctate keratitis, dystrophies, sarcoidosis, lupus erythematosus and pemphigus.

Three types of applicators are in general use. A radon bulb, known as the Burnam applicator, has been employed in the Wilmer Institute since 1927. From 200 to 500 millicuries is used, and, of course, the time of exposure is very brief. This is a great advantage when the physician has to hold the applicator in position for the full time of exposure. The skin erythema dose is 18 gram seconds.

The second type of applicator is a radium plaque. Fifty milligrams is spread thinly over the surface and a 0.1 Monel filter added. The radium-bearing surface measures 10 by 5 mm. A dose of 4 gram seconds can be given in ten minutes. With this applicator it is possible to use a shield of 0.5 mm. of sheet lead to block out the unneeded part of the surface of the applicator.

The radium D applicator consists of a circular plaque with a radium-bearing surface of 5.6 mm., and a filter of 0.05 mm. of aluminum has been devised. A two minute contact application gives a dose of 5 gram seconds. An applicator containing 50 mg. in two layers of 30 and 20 mg., respectively, with an active surface of 10 by 5 mm. has been recently manufactured.

Summary.—1. With beta radiation most of the dose can be limited to the first or second millimeters of tissue.

2. The nerves, muscle, bone and cartilage in the region of the eye are resistant tissues, which are not likely to be damaged by this radiation.

3. Excellent results have been obtained in many ocular diseases which have been difficult to treat with other agencies.

4. New types of applicators are available which simplify treatment.

DISCUSSION

Dr. Arthur M. Yudkin, New Haven, Conn.: What experience has Dr. McKee had with papilloma at the junction of the conjunctiva and cornea?

Dr. Frederick H. McKee: I have had no experience in treating papilloma of the cornea, but I treated two papillomas of the conjunctiva with beta radiation and found that these caustic rays successfully destroyed the lesions.

Dr. Frank A. Vesey (by invitation): Has Dr. McKee had any experience with xanthelasma?

Dr. Frederick H. McKee: Xanthelasma is a radioresistant lesion and the only one which I recall treating did not respond to the technic used at that time.

Choroiditis Proliferans (Charles H. May Memorial Lecture).
Dr. Adalbert Fuchs, Vienna, Austria (by invitation).

Dr. Fuchs described a new type of ocular disease and called it choroiditis proliferans. It is characterized by whitish striated bands,

which end in flamelike attenuations and are situated beneath the retina. Such strands appear occasionally as the sequel of retinal detachment and also in von Hippel's disease (angiomatosis of the retina).

Dr. Fuchs encountered 6 cases of this rare disease in China. In 1 patient the condition developed after a gunshot wound, and in the other 5, most of whom apparently had Harada's disease (acute exudative uveitis), it followed retinal detachment. In 2 patients the disease was binocular. As a rule, vision was very poor, but one boy had vision of 6/10. Nearly always thin, whitish strands, with knot-shaped enlargements, crossed the fundus, and frequently large areas of the fundus were covered by a whitish film, apparently connective tissue, which hid the structure of the choroid. The last case was apparently a combination of Harada and Vogt-Koyanagi disease, and the strands behind the retina were evidently pigmented in parts and appeared slate gray and whitish.

In no case was microscopic examination made. But in a case of metastatic carcinoma of the choroid the changes apparently represented the clinical manifestation of choroiditis proliferans: Cross sections of fine filaments of organized fibrin, running through the subretinal space, corresponded to the whitish strands which later are pressed against the choroid by the replaced retina. A thin layer of connective tissue between pigment epithelium and subretinal fluid was apparently the equivalent of the tissue which in choroiditis proliferans produces the wide, white discoloration of the choroid.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

Edwin B. Dunphy, M.D., *President*

Merrill J. King, M.D., *Secretary-Treasurer*

Regular Meeting, March 17, 1948

CASE PRESENTATION

Cases were presented of the following conditions: (1) dislocated lenses in a young boy, the lens in one eye being in the anterior chamber; (2) iridodialysis and traumatic edema of the retina resulting from a BB shot, the bullet having been recovered from the lower cul-de-sac; (3) ascending myelitis and blindness in a young woman, the visual defect consisting of complete amaurosis in one eye and a defect in the lower nasal field of the other eye at the onset, with subsequent transformation into homonymous hemianopsia; (4) detached retina, which had been successfully operated on five weeks previously by Dr. Schepens with a partially penetrating scleral resection (scleral infolding); (5) corneal scarring from multiple foreign bodies, and (6) nystagmus and palsies of cranial nerves associated with recurrent medulloblastoma of the cerebellum.

PRESENTATION OF PAPERS

Glaucoma. Dr. Paul A. Chandler, Boston.

This lecture, the fourth in a series on glaucoma, was concerned chiefly with the type of glaucoma which follows intraocular inflammation or injury. The author pointed out that a rise in tension secondary to acute iritis does not always necessitate surgical intervention. Pressures as high as 40 mm. of mercury (Schiøtz) may be tolerated for at least one week. The medical treatment of choice is epinephrine collyriums. The surgical procedure of choice, when indicated, is keratome paracentesis, followed within twenty-four hours by vigorous massage.

The treatment of glaucoma with low grade uveitis varies according to the activity of the inflammation. Miotics are indicated only so long as the eye shows no active inflammation and there are no posterior synechias. Cyclodialysis and filtering operations are less satisfactory in this type of glaucoma than in primary glaucoma. Cyclodiathermy may be necessary as a last resort. With blocked pupil (iris bombé) it is important not to operate so long as the tension is normal or less than normal. When the tension is elevated, the best surgical procedure is transfixion of the iris, followed by a large basilar iridectomy when the eye is quiescent. The latter, however, is contraindicated when there has been long-standing uveitis, as in sympathetic ophthalmia.

Glaucoma following contusion is usually transient and can be treated with miotics. The blood clot may be satisfactorily removed by a simple paracentesis if necessary. In the case of delayed hemorrhages, in which the blood is black and the tension is very high, removal of the clot is necessary to prevent hematogenous pigmentation of the cornea. This may be accomplished by inserting the irrigating nozzle through a wound at the limbus and expressing the clot.

Importance of Examination of the Ora Serrata in Cases of Retinal Separations. Dr. C. L. Schepens and Dr. G. C. Bahn, Boston.

The authors described the appearance of the ora serrata as seen ophthalmoscopically and discussed the methods by which it could be best visualized. There is least distortion by indirect ophthalmoscopy with a + 20.00 D. lens.

They noted some of the more significant findings in cases of detached retina. The vitreous often shows circular bands of condensation; in cases of aphakia in which no hole is readily found, there are frequently many small disinsertions, which at first simulate the normal ora serrata. Meridional bands may sometimes overlie the projections of the ora serrata. These are possibly early manifestations of proliferating ciliary epithelium and may give rise to small retinal tears.

Ocular Signs Associated with Head Injuries. Dr. Frank B. Walsh, Baltimore.

Head injuries may result from direct trauma, from contrecoup effects, from crushing injuries and from gunshot wounds. The symptoms which are of value in determining the prognosis are the state of consciousness,

the pulse rate, the respiratory rate, the temperature, the presence of convulsions and the size of the pupils. The injuries to the cranial nerves may result from division of the nerve, from bruising of the nerve, from interference with the blood supply locally, from local pressure on the nerve, from fracture of adjacent bone or from torsion of the brain stem. Loss of vision due to injuries to the optic nerve probably results from indirect injury to the nerve, rather than to hemorrhage or section of the nerve. The loss of vision is usually immediate with some recovery of vision in three or four hours and maximal recovery in three to four weeks.

SOCIETÉ FRANÇAISE D'OPHTALMOLOGIE

Fifty-Fifth Annual Meeting, Paris, May 21-25, 1948

As usual, a considerable number of foreign members came for the occasion, and the United States was represented by Paton, Castroviejo, Loutfallah and Albaugh.

The annual symposium, this year on "Corneal Transplantation" was conducted by Paufigue, Sourdille and Offret. Keratoplastic surgery is arousing more interest than ever in France since the new law came into effect early this year which permits the eyes to be removed from dead people at once, and without the twenty-four hour delay previously required. This provision supplies French ophthalmologists with much needed raw material. It is difficult to review this symposium, contained in an excellent volume of 360 pages, with many illustrations and color plates. It covers keratoplasty thoroughly and should be read in full. Probably the most interesting feature for American ophthalmologists is the prominent place given to partial (or lamellar) keratoplasty. This has been warmly advocated in France, mainly by Paufigue, who claimed that in many cases as good results can be obtained by removing one half or three fourths of the thickness of the cornea as with total removal. The operation is more difficult to perform but entails less risk. It is surprising to see how the transparent transplant has a favorable effect on the neighboring opaque tissues, which gradually clear up in many instances. Total removal of the cornea (in full thickness) was performed in a few cases by Sourdille, who stated the belief that this type of operation may have a future in chosen cases.

Just previous to the meeting in Paris, a short one was held in Nantes, where corneal transplantations were performed by Sourdille (Nantes), Paufigue (Lyon), Lapointe (Montreal), Arruga (Barcelona), Babel (Geneva), Venco (Pavia) and Paton and Castroviejo (New York). During the discussion which followed the symposium, Mercier (Tours) reported satisfactory results he had obtained in a case of late opacification of the transplant (after nine months) by means of an implant of subconjunctival placenta.

De Saint Martin (Toulouse) used similar implants in cases of progressive and complicated myopia and claimed that 75 per cent of his 36 patients had had some improvement of visual acuity.

Altogether, over 60 papers were read, most of them interesting, and it is difficult to make a choice. As usual, the discussion on cataract surgery was lively. No topic ever seems to be as loaded with emotion as this one. This year the discussion started with a fine film by Roger Rossano (Paris) showing his technic and with a paper by De Saint Martin (Toulouse), stressing the importance of corneoscleral sutures for safety and for less astigmatism. This would seem a noncontroversial statement nowadays, but an ophthalmologist took the floor, claiming that conjunctival sutures were still to be preferred, since corneoscleral sutures were more difficult to place, implied longer and severer manipulations and entailed added danger of loss of vitreous. The same man stated the belief that a low degree of astigmatism was more advantageous to the surgeon's statistics than really beneficial to the patient, but this statement was sharply denied by the majority. There was a moment of pleasant relaxation with a good laugh brought forward by a surgeon who stated that if astigmatism was high at first it decreased slowly and gradually, and that in his experience it was almost negligible when his patients were reexamined thirty years later.

Beauvieux and co-workers (Bordeaux) observed optic nerve atrophy in 2 patients treated with streptomycin. Pesme (Bordeaux) and Delbes (Perigueux) published the first case of ocular toxoplasmosis seen in France. Schiff (Lausanne) reported on a case of corneal and conjunctival cystinosis, a rare disease. (The reviewer reported a short time ago another case with cystine crystals in the vitreous.) Desvignes and Rimey (Paris) stated the belief that a careful study, with fluorescein, of the blood-aqueous permeability in the healthy eye (in case the other was wounded) may give an early warning of impending sympathetic ophthalmia. The Calmettes and co-workers (Toulouse) spoke of Sjögren's disease. They stated the belief that vitamin A deficiency and liver deficiency are important factors in its development, as is also ovarian imbalance. They had favorable results in their patient, a woman of 66, with estrogen therapy. Weekers (Liége) brought a statistical survey of 2,031 cases of retinal detachment, showing that the incidence was higher in spring and summer. This might tend to prove that increased illumination is a provocative factor. Fritz (Brussels) stated the belief that an increase in the capillary pressure is accountable for many cases of primary simple glaucoma, with the consequent leakage of proteins through the capillary walls. Balavoine (Geneva) advocated early operation in cases of congenital glaucoma (repeated anterior sclerotomy with opening of the angle). Zanen and Brihaye (Brussels) reviewed 35 cases of altitudinal hemianopsia from the literature and published 3 new ones of opticochiasmatic arachnoiditis. They believe that in the latter disease the altitudinal field defect is not due to direct pressure by the arachnoidal bands or cysts, but, rather, is caused by vascular strictures. Gassenc and Cazaban (Montpellier) have experimented successfully with intra-aqueous injections of drugs (pilocarpine, atropine, yohimbine and ephinephrine). Dubois (Paris) observed a Rayleigh type of color anomaly in a patient who had a macular lesion. Renard and Bregeat (Paris) have employed with success a modified

Filatov placenta implant; they use fresh placenta soaked in penicillin for thirty minutes. The reaction is sometimes intense, but they claimed better results with it than with aged and dried placenta.

As usual, operative demonstrations were arranged for during the meeting. On one afternoon the congress was invited to visit the Bibliotheque Nationale, where they were shown rare manuscripts which are not usually visible. That evening there was the annual dinner, presided over by Dr. Lapointe, of Montreal. There were numerous postprandial speeches, chiefly by the foreign members present. There was also one by Dr. Merigot de Treigny, which was a farewell speech, since he has, unfortunately, resigned this year as secretary general of the society.

EDWARD HARTMANN, M.D.

Fifty-Sixth Annual Meeting, Paris, May 22-26, 1949

The gathering had, as usual, a strikingly international aspect, more than half the members of the society being foreign and a great number being in the habit of coming to Paris at the time of the annual May meeting. American ophthalmology was represented by Dr. Daniel B. Kirby, of New York, and his fine film illustrating his method of cataract extraction.

The annual symposium, conducted by Dr. Marcel Kalt, was entitled "Hypertensive Uveitis." The papers comprising this symposium, forming a volume of about 400 pages, with beautiful colored illustrations, had been sent to the members a month ahead of time, and the discussion, after Dr. Kalt's presentation, was long and interesting.

Fifty-three other papers were read. The most important are summarized here. F. Rouher (France) advocated the injection of air in the anterior chamber in the treatment of penetrating wounds of the eye. S. de Vries (Netherlands) reported on aqueous veins, with fine photographs. Bernard Streiff (Switzerland) showed the appearance with the slit lamp of a corneal microfilaria. Frank Law (England) had pertinent comments on a case of cellulitis of the orbit: The general symptoms were alleviated with penicillin, and this improvement was responsible for delay in the surgical treatment, with consequent damage to the optic nerve. Archimeda Busacca (Brazil) stressed that the base of the corneal epithelium is distinct from Bowman's membrane. He also gave excellent illustrations of a slit lamp study of the vitreous with Goldmann's contact lens. Louis Paufique and Gabriel Sourdille (France) both stressed the therapeutic value of lamellar corneal transplants. Gabriel Renard and Paul Bregeat (France) read a paper on the possible relation of recurring vitreous hemorrhages, retinal degeneration and the diencephalon. Georges Farnarier (France) gave a report on 2 cases of toxoplasmosis (this disease has only recently been recognized in France). Eugene Wolff (England), in a paper on Coats's disease (retinitis exudativa), claimed that the process usually is an exudative choroiditis. There were encouraging reports by

Toulant (Algeria) and A. Larmande (France) and by Pesme (France) on the treatment of sympathetic ophthalmia with penicillin. The first authors stressed the frequency of disseminated choroiditis with small round white spots in this disease. Babel and Monnier (Switzerland) used electroretinography in studying the critical fusion frequency. Lukic and Savic (Yugoslavia) claimed that neurologic symptoms (mainly hypothalamic) could be found in a fair proportion of myopic patients. Spiro Spyratos (Greece) gave a report on ocular symptoms related to undernourishment in Greece during the war years. J. Marie Habig (Belgium) read a paper on African trypanosomiasis and its ocular complications. Pierre Desvignes (France) stated that diplopia was often the first symptom of toxic complications in streptomycin treatment. Adrien Fritz (Belgium) claimed excellent results from suturing a contact glass over the eye after operation, such as cataract extraction or corneal transplantation. M. E. Alvaro (Brazil) read a paper on beta ray therapy in ophthalmology. Paul Bregeat and David (France) stressed the value of opening the optic canal in treatment of edema of the optic nerve.

The scientific meetings were held every morning, and there was in the adjoining hall an exhibit of instruments, apparatus and drugs used in ophthalmology. On two afternoons there were operative demonstrations in the various hospitals in Paris. Keith Lyle, of London, gave an interesting talk at Lariboisière Hospital on the orthoptic treatment of strabismus, and several presenters showed surgical films: Dr. G. Tessier, of Paris; Dr. J. E. Converse, of New York; Dr. Louis Paufique, of Lyons; Dr. Gabriel Sourdille, of Nantes; Dr. Jean Baptiste Coppez, of Brussels, and Dr. Enrico Grancini, of Milan.

On one afternoon there was an excursion to the Château de la Malmaison, with its Napoleonic souvenirs, followed by a reception given by Dr. Gabriel Renard in his nearby country house. On that same evening the usual banquet was held; this was a great success, with almost 300 guests attending.

In 1950, the meeting of the society will not be held in May, as usual, but in July (23 through 27), just after the International Congress held in London (July 17 through 21). This change was made so as to enable ophthalmologists to come to Paris after London. As secretary general of the French Society of Ophthalmology, the author of this review wishes to extend a hearty welcome to all those who would like to come to the meeting in Paris.

EDWARD HARTMANN, M.D.

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

T. Keith Lyle, *Honorary Secretary*

Sixty-Eighth Annual Congress, April 8-10, 1948

The Sixty-Eighth Annual Congress of the Ophthalmological Society of the United Kingdom was held on April 8, 9 and 10, 1948, at the Royal Society of Medicine, London. Over 200 members and many

distinguished Continental visitors were present, among whom were Prof. Marc Amsler, Prof. J. W. Nordenson, Prof. H. Ehlers, Prof. J. van der Hoeve, Dr. E. Pflüger, Prof. E. Velter, Prof. H. J. M. Weve, Prof. A. Franceschetti, Prof. M. Appelmans, Prof. W. H. Melanowski, Dr. H. Sjögren, Dr. T. L. Thomassen and Dr. A. C. Copper.

After a short opening speech by the president, Dr. A. J. Ballantyne, the topic for the morning's discussion, "Subjective Disorders of Vision" (excluding those due to local ocular disease), was introduced by Prof. H. Cohen in a communication that was interesting, well balanced and beautifully delivered. He was followed by Dr. Denis Williams, who also contributed original and important observations on the nature of "macular sparing," showing an enviable mastery of the more recondite methods of perimetry, and by Mr. J. H. Doggart, who continued ably and agreeably on this interesting subject. The discussion that followed could not maintain the high level of excellence that marked the opening speeches. A number of observations, interesting and sometimes entertaining, were offered.

The Bowman Lecture was delivered this year by Prof. Marc Amsler. The subject chosen was "New Clinical Aspects of the Vegetative Eye," a clear and impressive thesis on the clinical and scientific value of biochemical and biophysical microanalysis of the aqueous fluid. This lecture was beautifully illustrated by a film. Evidence was also presented of the blood-aqueous barrier by the delay in appearance there of systemically administered fluorescein as seen with slit lamp microscopy in cases of chronic glaucoma, uveitis and systemic disorders. The bearing of this assessment of disease was illustrated.

The following papers were read during the Congress and covered a wide field:

"Ocular Palsies Due to Infection of the Nasal Sinuses," by Dr. Helen Dimsdale and Mr. D. G. Phillips. The authors emphasized with case histories the frequency of sinusitis as a cause of ophthalmoplegia, coincidentally through its toxic effect or as a result of pressure due to chronic sphenoiditis or to periostitis of the superior orbital fissure.

"A Preliminary Survey of Forty-Five Consecutive Cases of Congestive Glaucoma," by Mr. J. P. F. Lloyd. The author, concluded *inter alia*, that acute glaucoma does not often produce as acute symptoms as those classically described, that in cases with gross visual loss there may well be a thrombotic factor and that recurrences are rare, although gonioscopy shows obliteration of the angle of the anterior chamber after iridectomy. He stressed the inadvisability of using physostigmine after trephination and the fundamental difference between acute and chronic glaucoma.

"The Conjunctival Nevus and the Neurogenic Theory of Melanoma," by Mr. Eugene Wolff. The neurogenic theory of the origin of these tumors is discountenanced.

Pictorial Demonstrations by Dr. H. M. Traquat: "Spasm of the Central Retinal Artery," "Entoptic View of Retinal Vascularization," "Hypophysial Tumor Causing Homonymous Hemianopsia and Third Nerve Paralysis," "Depigmentation of Iris in Chronic Glaucoma." In

discussing these demonstrations, Mr. E. Kraupa described how it was possible to see two or three entoptic vascular shadows, with the use of two or three lights, and Mr. M. W. Paterson showed drawings of entoptic vessels that suggested a vascular raphe to the nasal side of the central avascular area.

"Venous Pressure in Glaucomatous Eyes," by Dr. T. L. Thomassen. By ocular tonometry and manometry of the episcleral veins, venous pressure was shown to anticipate a rise or fall of intraocular tension, the outflow of aqueous in aqueous veins being observed to be hampered as pressures increase, and vice versa.

"Clinical Perimetry," by Mr. G. I. Scott.

"Subconjunctival Rupture of the Globe by a Cow's Horn"; "Arteriovenous Aneurysm: Report of a Case," by Mr. G. T. W. Cashell. In the first case there was remarkable recovery of a disorganized eye, with avulsion of the iris in contrast to a case of total iridectomy effected by a jackdaw, seen at the clinical demonstration. Two cases similar to the latter were demonstrated by A. Franceschetti.

"Papilledema in Association with Toxic Hydrocephalus," by Mr. A. G. Cross. A follow-up study of 32 cases of toxic hydrocephalus showed only 1 case of optic nerve atrophy and 4 cases of arcuate extension of the blindspot, the results confirming the inadvisability of early decompression.

"Latent Nystagmus," by Mr. T. Keith Lyle. Six case histories of this condition in association with concomitant squint were presented, with emphasis on the importance of testing binocular vision and the undesirability of occlusion in such cases. A film was shown.

"Classification of the Unassociated Dystrophies of the Fundus," by Prof. Arnold Sorsby.

Pictorial Demonstrations by Mr. J. Ellison: "Pressure Grafting in the Contracted Socket with Plunger Anchored to a Dental Cap-Splint," "Epibulbar Dermoid," "Gummatous Ulceration of the Eyelids."

"Prognosis in Detachment of the Retina," by Mr. C. Dee Shapland. An analysis of 155 cases was presented.

"Mode of Development of the Vascular System of the Retina with Observations on Its Significance for Certain Retinal Diseases," by Dr. I. C. Michaelson. Retinal vessels originate by budding from other vessels, the capillaries arising from veins, and not from arteries; hence, in diabetes the veins and capillaries are principally affected; in hypertension, the arteries.

"Atropine in Treatment of Glaucomatous Iridocyclitis," by Prof. W. H. Melanowski. Six cases were discussed.

"Autoeversion of the Upper Lids," by Mr. W. C. Souter. Presentation of a film with anatomic discussion furnished an agreeably light note for the conclusion of the Congress.

A joint clinical meeting was held in association with the ophthalmologic section of the Royal Society of Medicine at the new Institute of

Ophthalmology, and cases of interest were presented by Dr. Mary Cripps, Mr. A. G. Cross, Mr. A. C. L. Houlton, Mr. E. F. King, Mr. T. Keith Lyle, Mr. S. Philps, Mr. H. Ridley and Mr. P. Trevor-Roper.

A trade exhibition of ophthalmic instruments was also held during the Congress.

The annual dinner of the Society was held at the Royal College of Surgeons by kind invitation of the president and council of the College. Prof. Henry Cohen proposed the toast of the Society with polished urbanity, and the president replied.

CORRECTION

In the article by Dr. Hugh C. Donahue entitled "Migraine and Its Ocular Manifestations," which was published in the January 1950 issue of the ARCHIVES, the following corrections should be made:

On page 109, line 25, "syndrome of anoxia" should read "syndrome or anoxia"; on page 125, line 17, and on page 127, line 22, "54 per cent" should read "34 per cent."

This article was a thesis accepted by the Committee on Theses of the American Ophthalmological Society in partial fulfilment of the requirements for membership.

E. B. Meyrowitz

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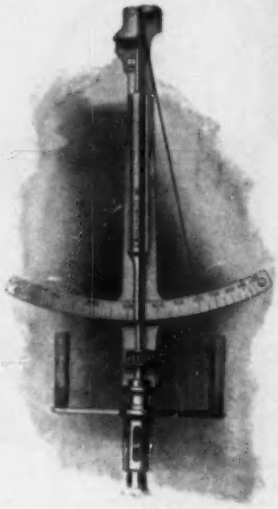

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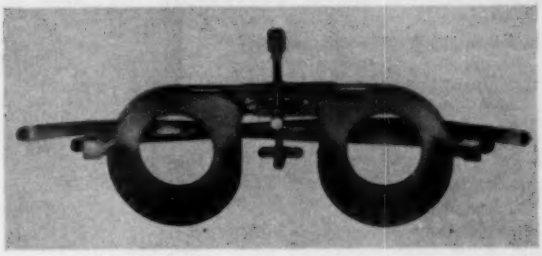

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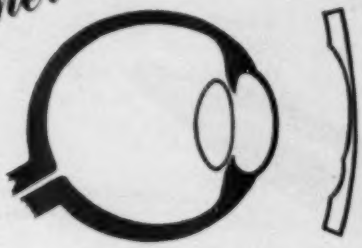

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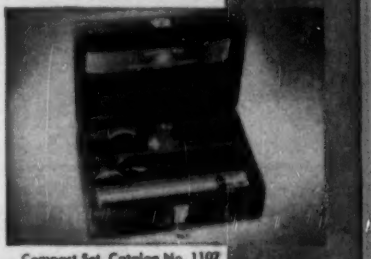

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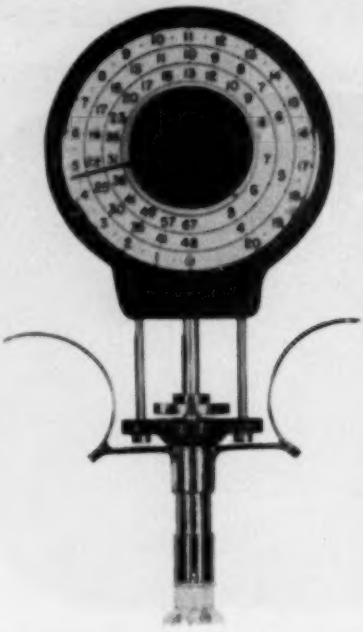

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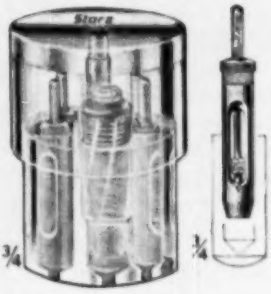

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